

FIG. 1

BEST AVAILABLE COPY

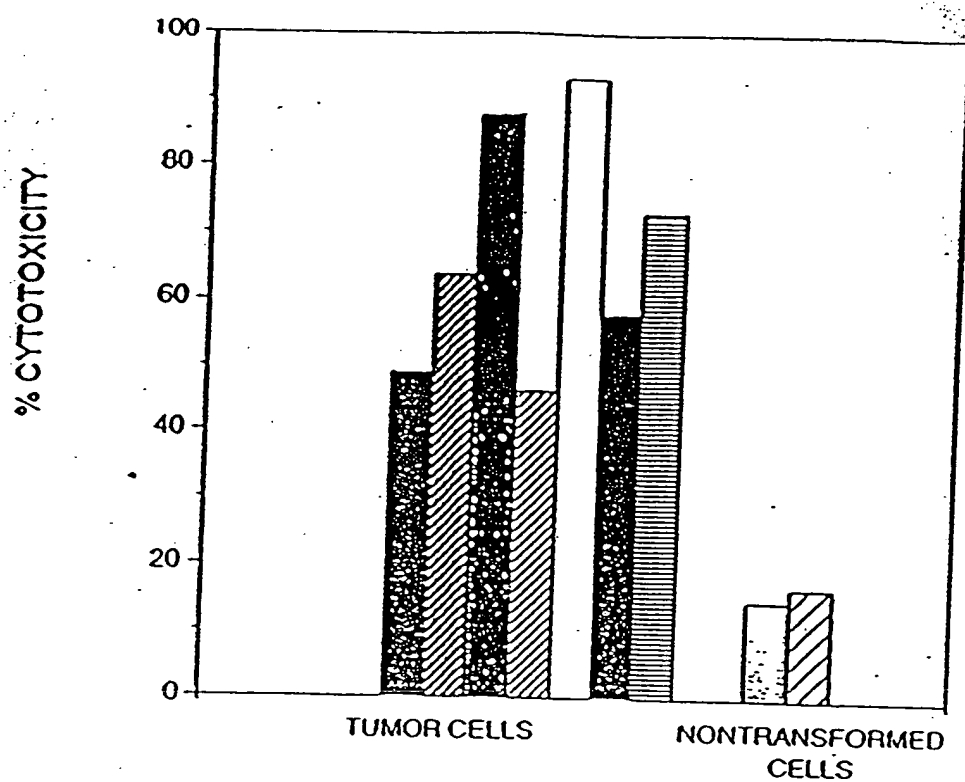
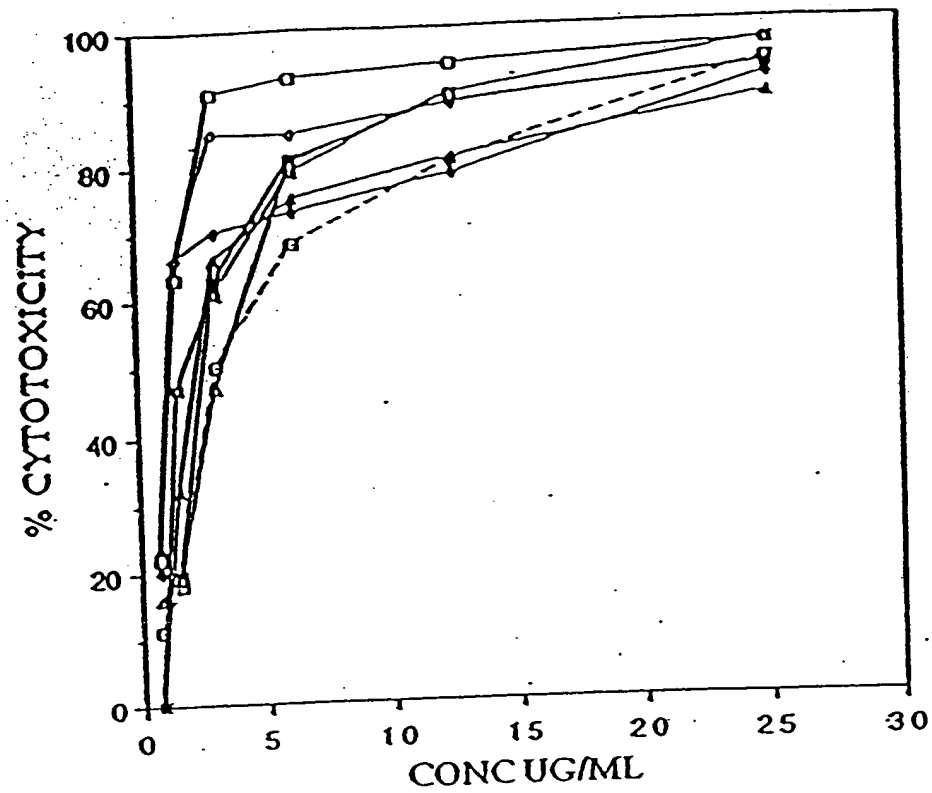


FIG. 2



---○--- HEY
—●— OVCAR-3
—□— C-1
—◇— SKOV-3
—▲— PANC-1
—◻— 769-P
—△— 786-O
—▽— A498

FIG. 3

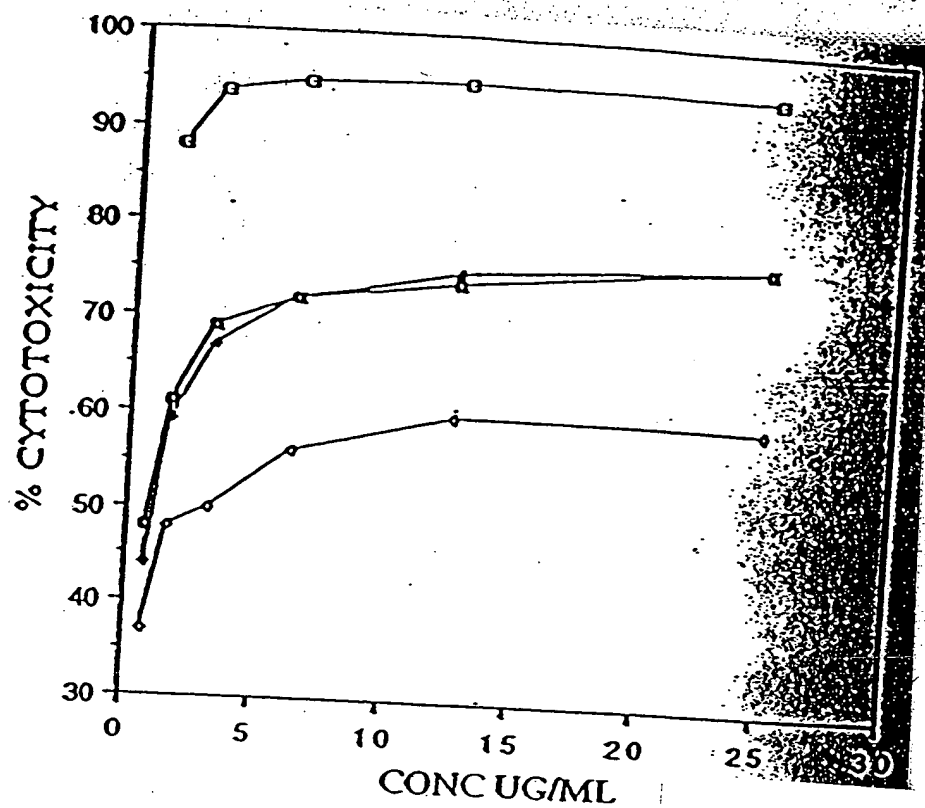
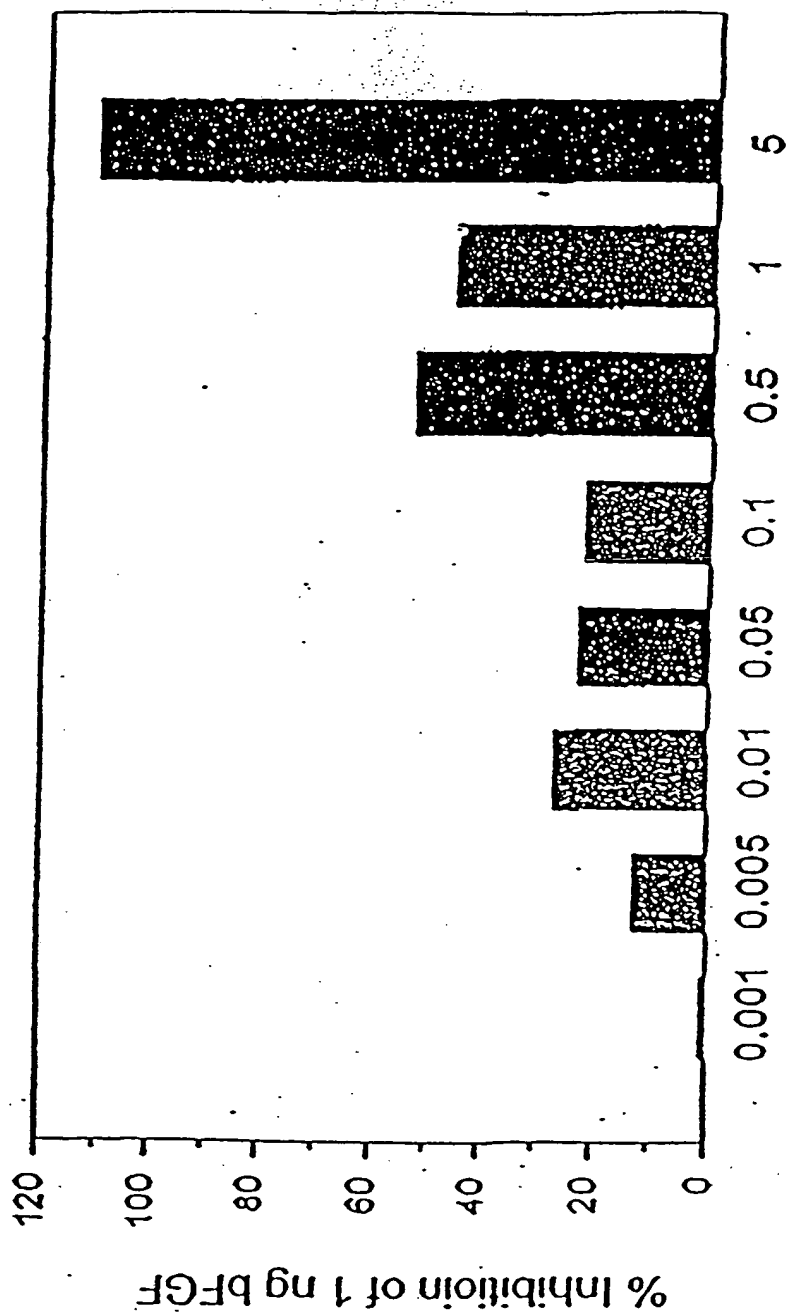


FIG. 4



UA-BRF-004-DELEP F035 $\mu\text{g/ml}$

FIG. 5

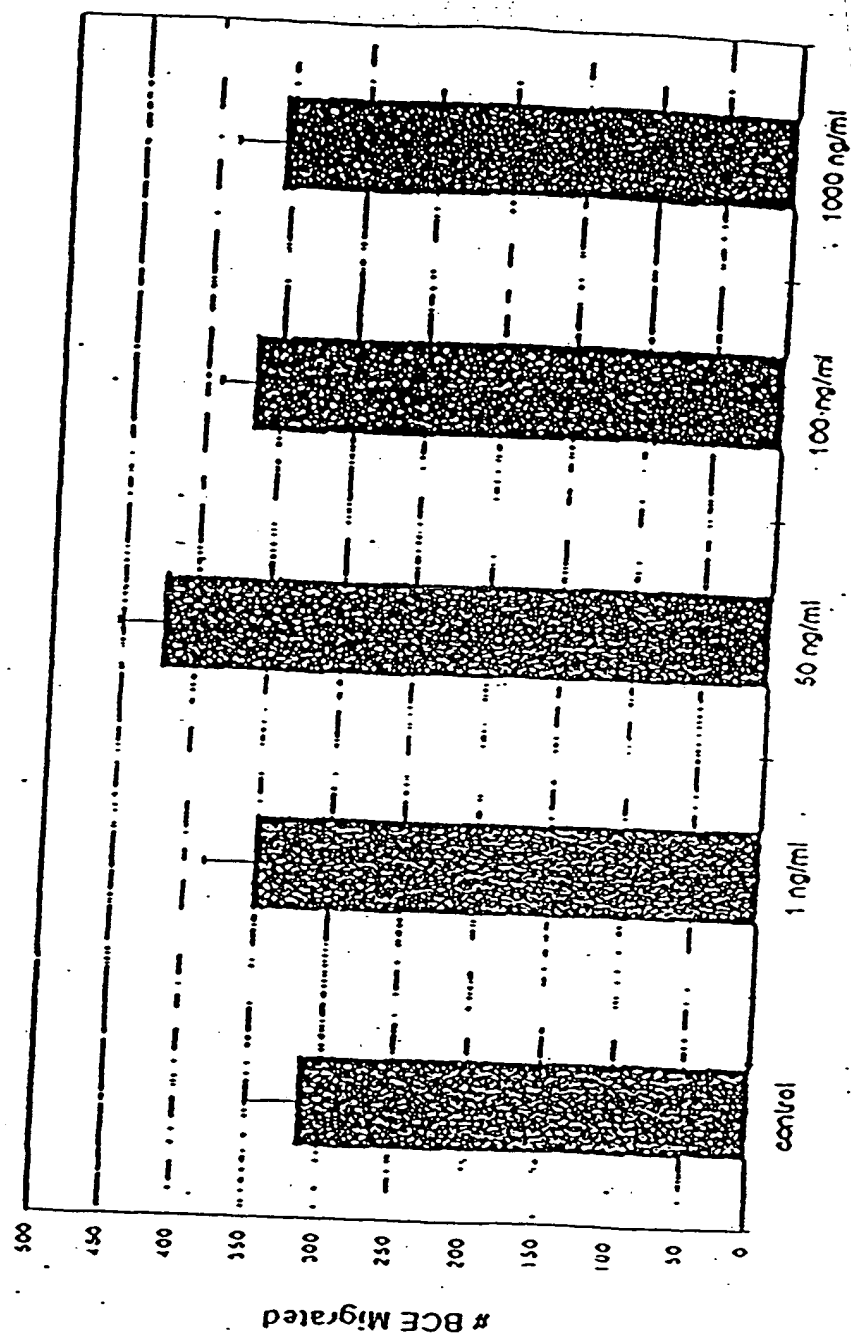


FIG. 6

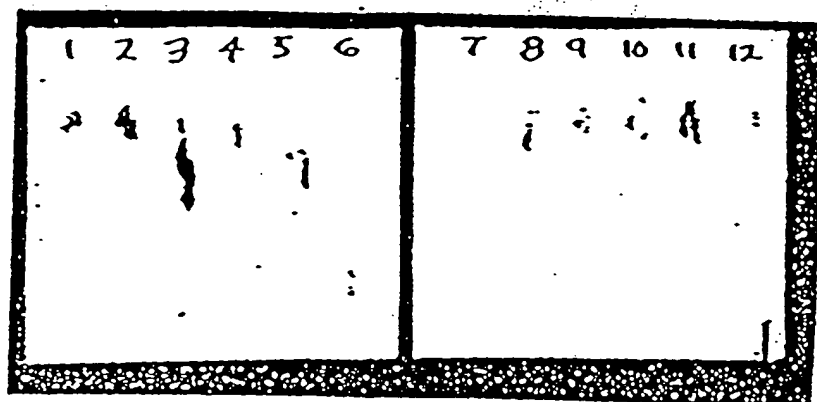


FIG. 7



FIG. 8

Dose: 0.2 ml

ACETONE
4 weeks

Mouse # 133

FIG. 9A

Dose: 0.2 ml

ACETONE
8 Weeks

Mouse # 150

FIG. 9B

Dose: 100 nmol

DMBA
4 Weeks

Mouse # 420

FIG. 9C

Dose: 100 nmol

DMBA
8 Weeks

Mouse # 420

FIG. 9D



Dose: 0.3 mg

Compound # 35
4 weeks

Mouse # 136

FIG. 9E

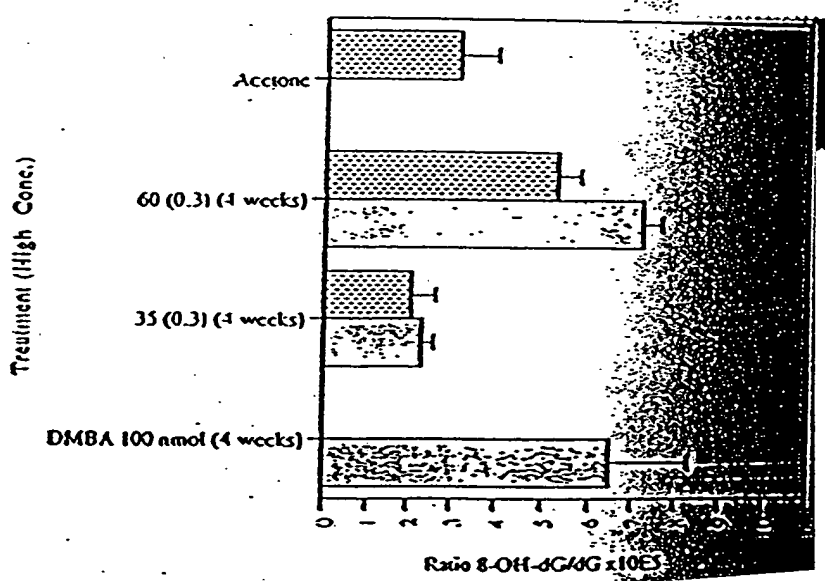
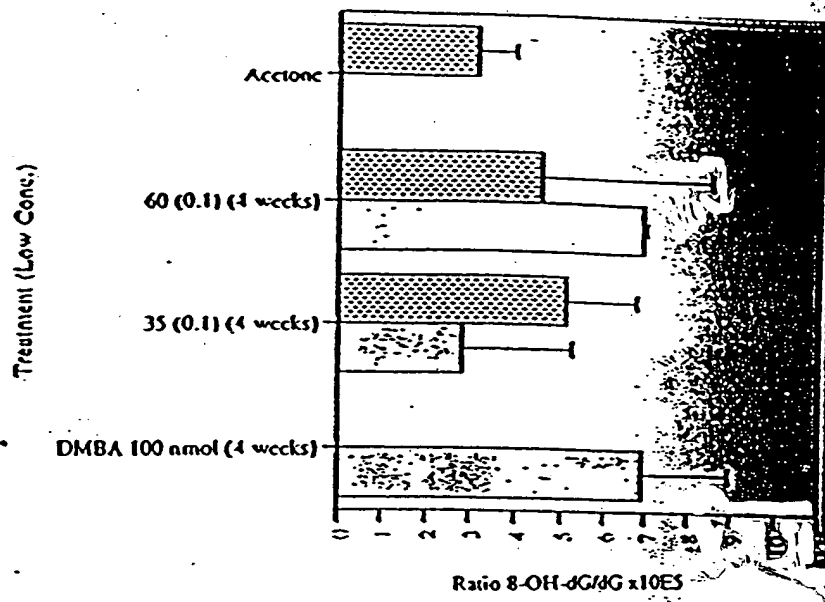
Dose: 0.3 mg

Compound # 35 + DMBA
8 Weeks

Mouse # 140

FIG. 9F





▨ -DMBA
□ +DMBA

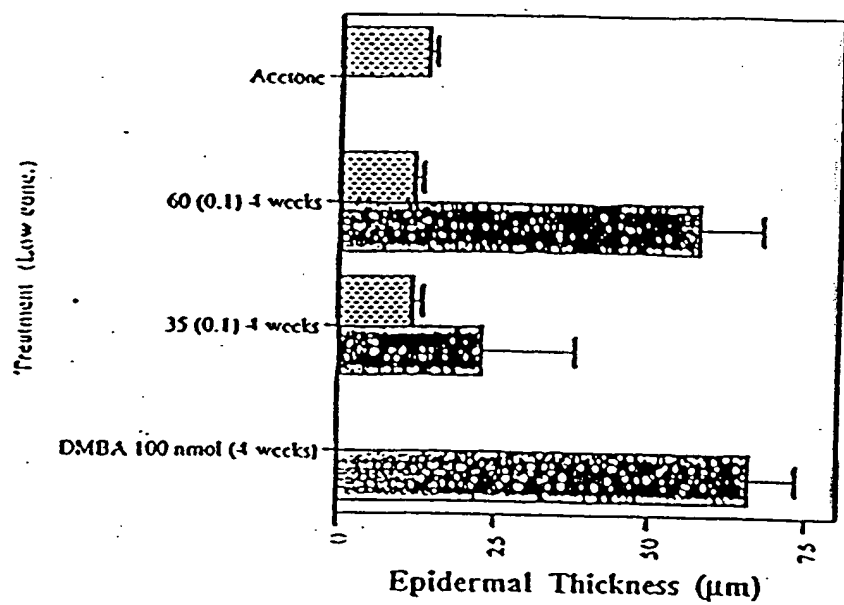


FIG. 11A

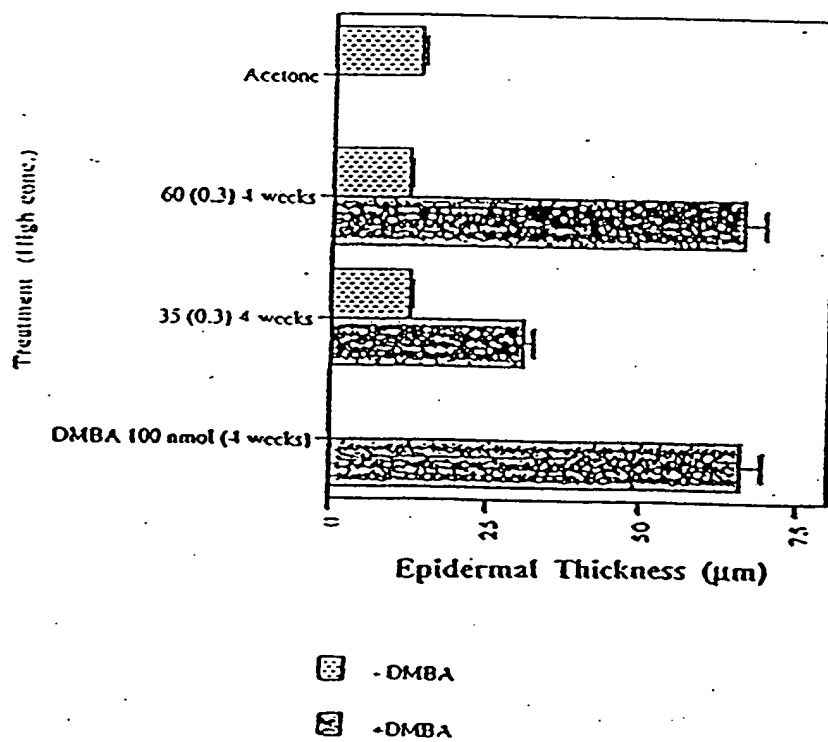


FIG. 11B

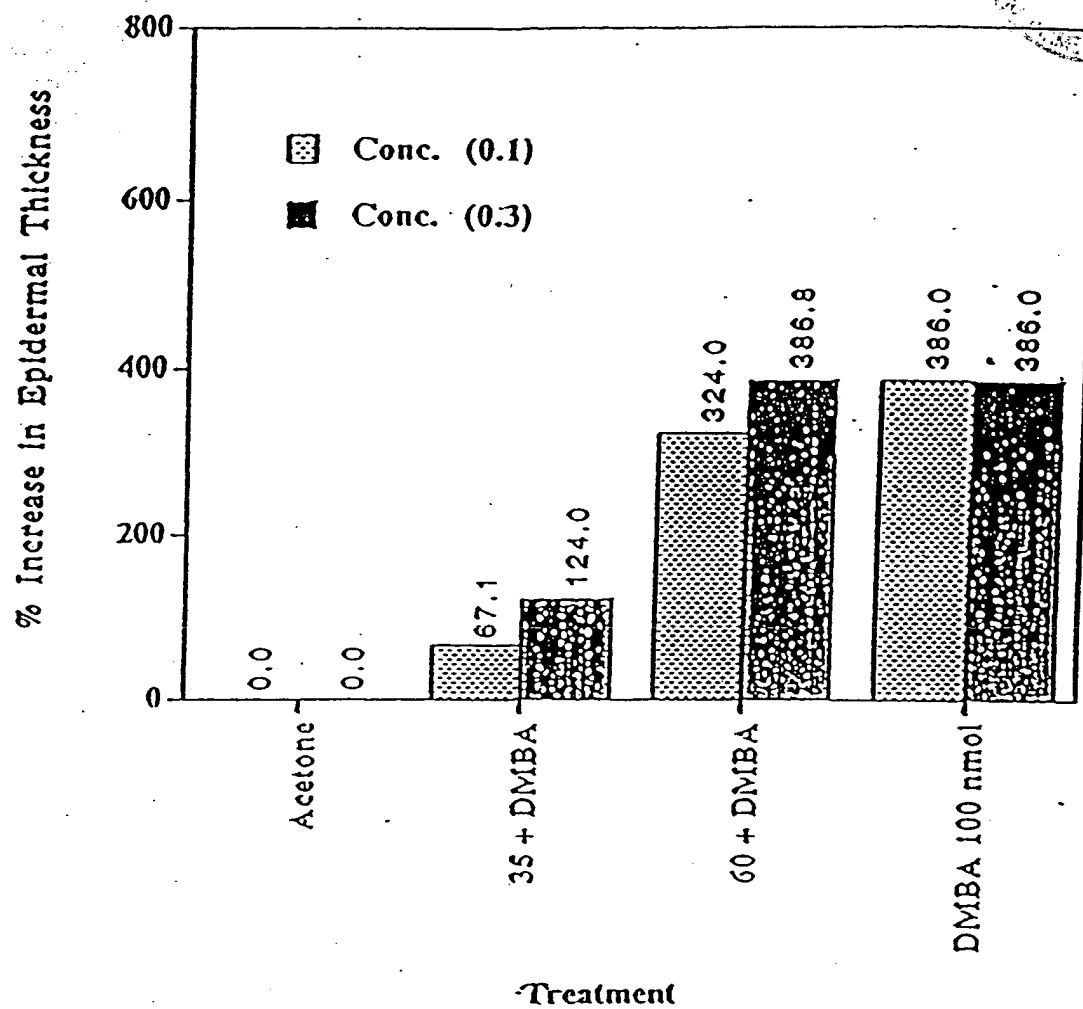


FIG. 12

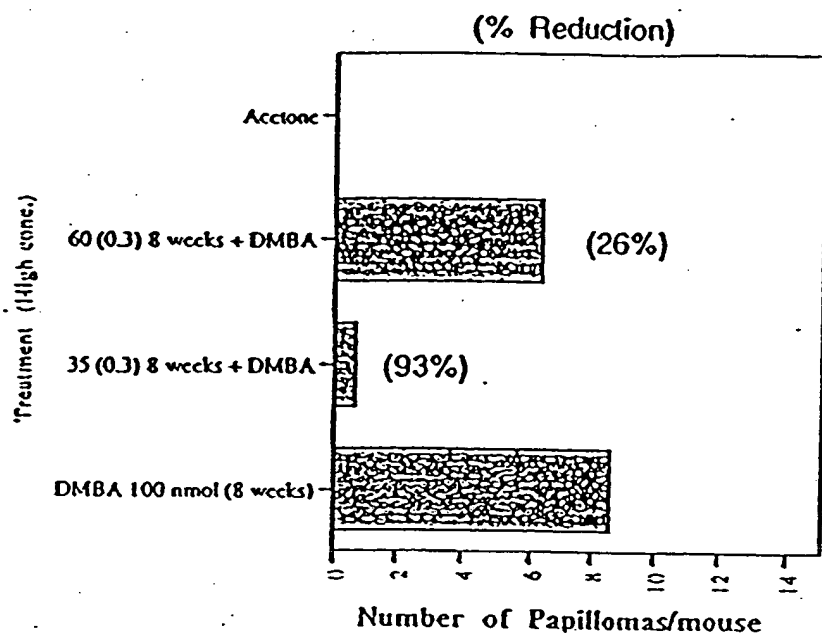


FIG. 13

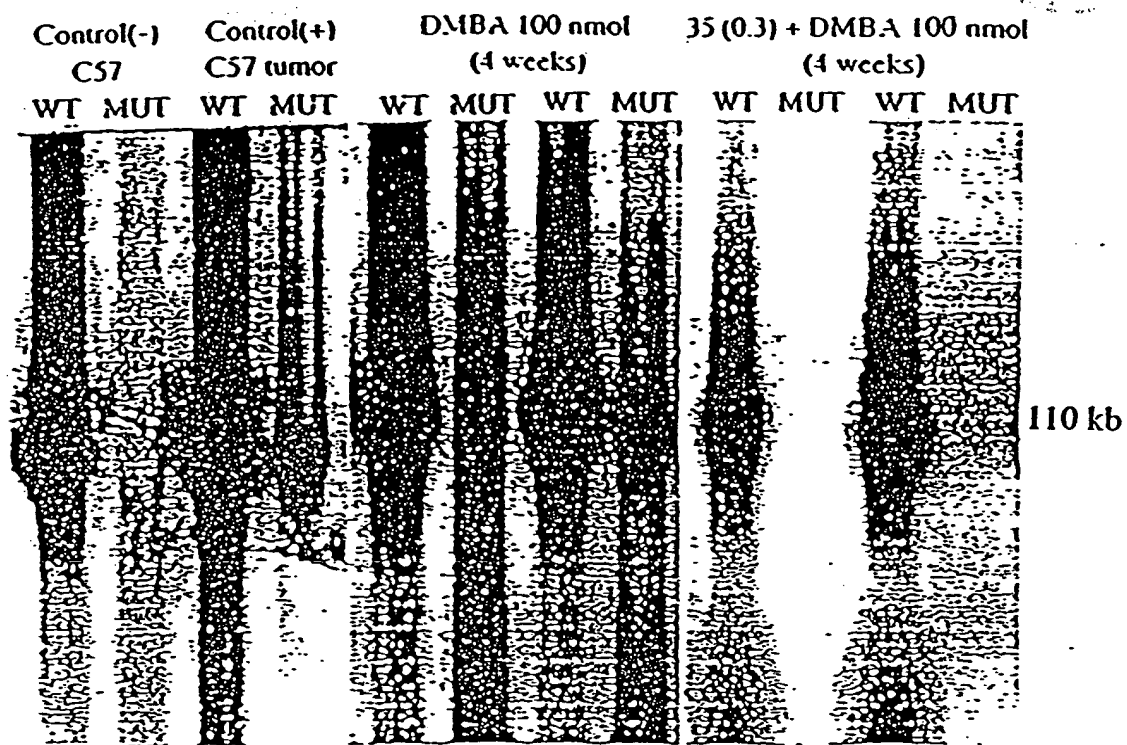


FIG. 14

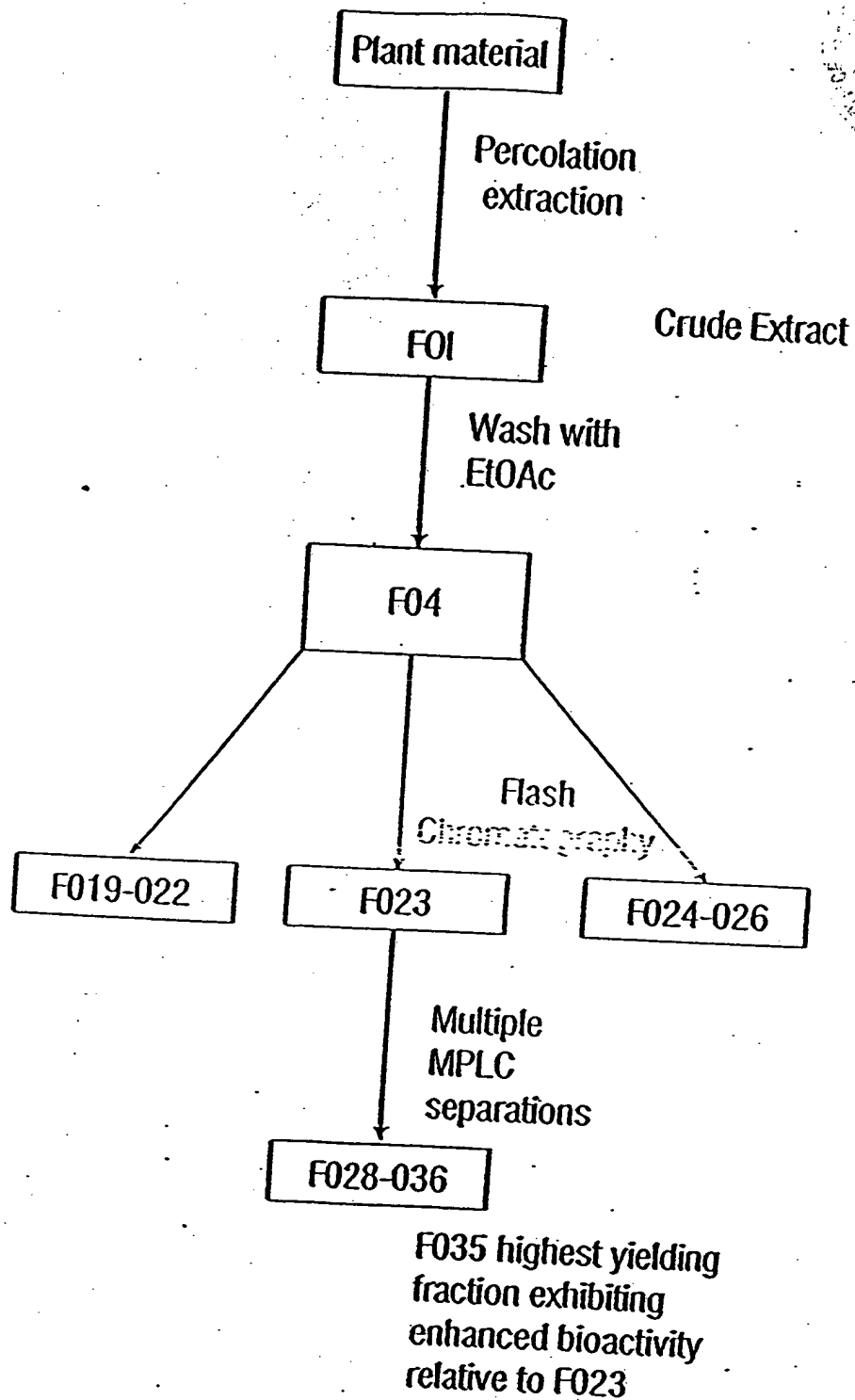


FIG. 15

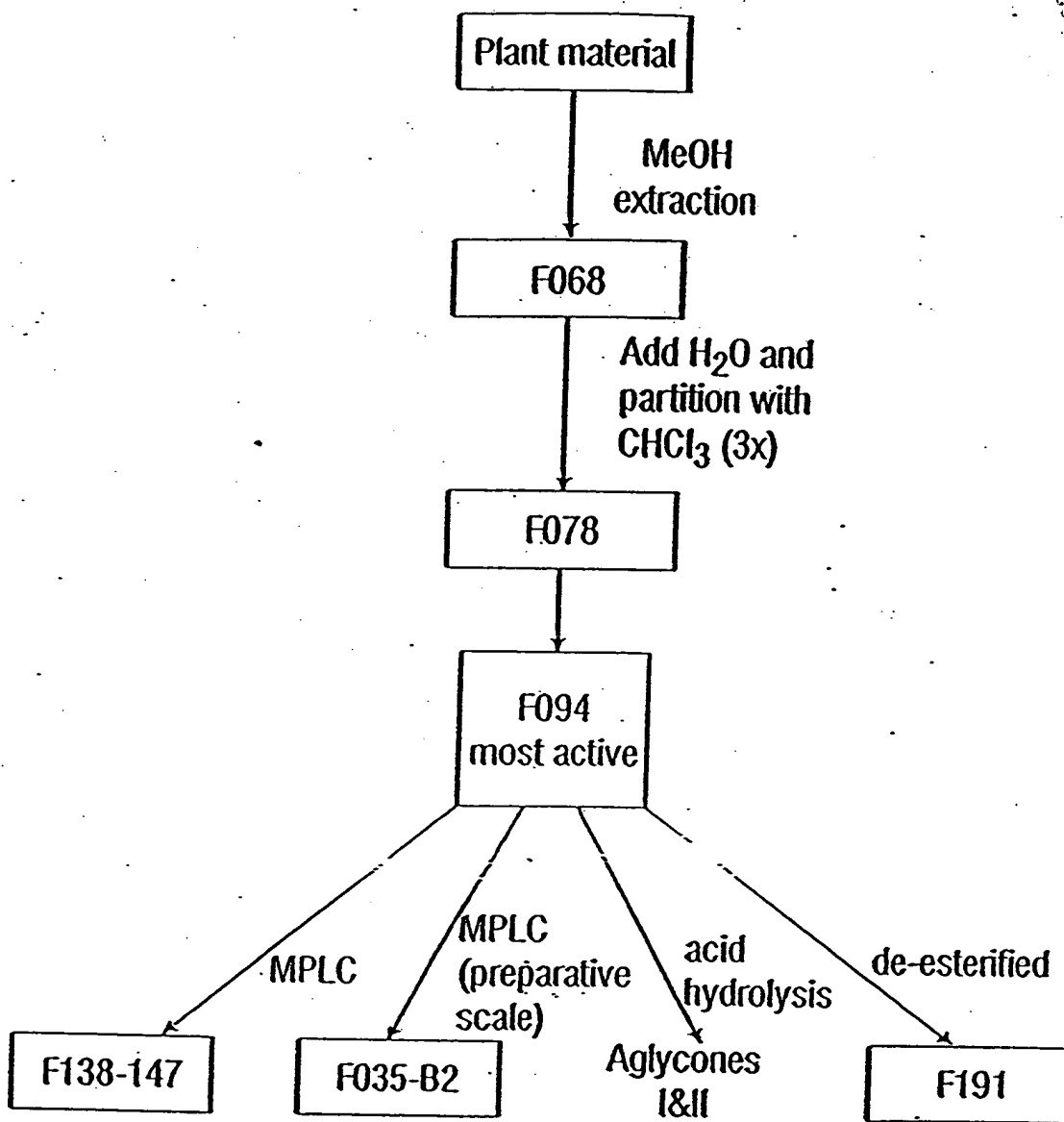


FIG. 16

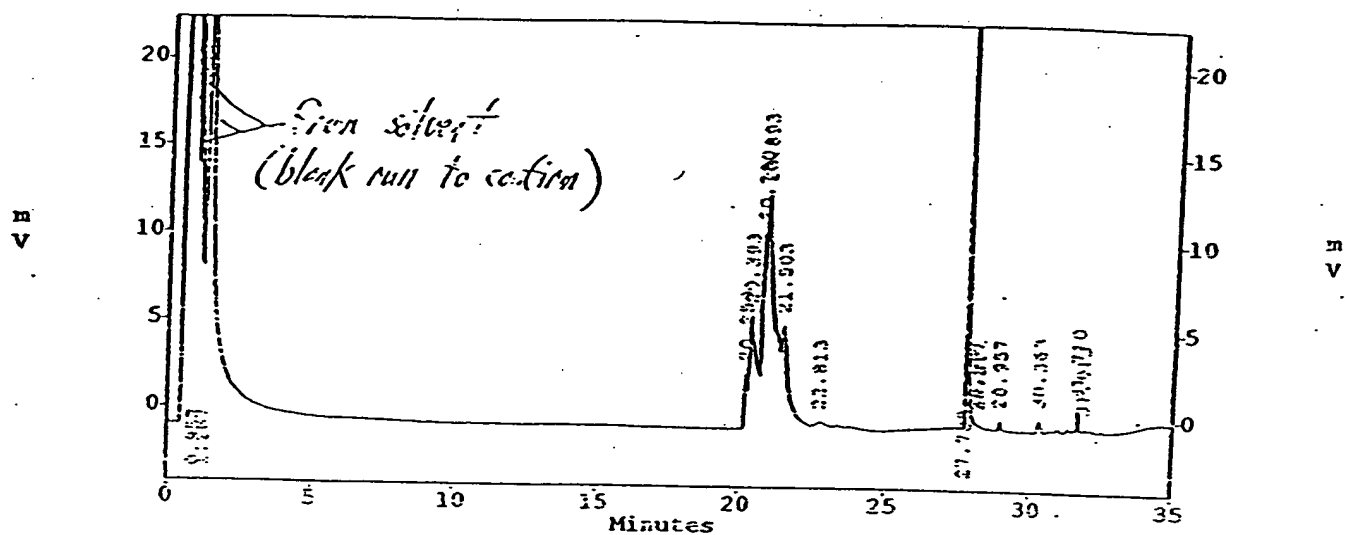


FIG. 17A

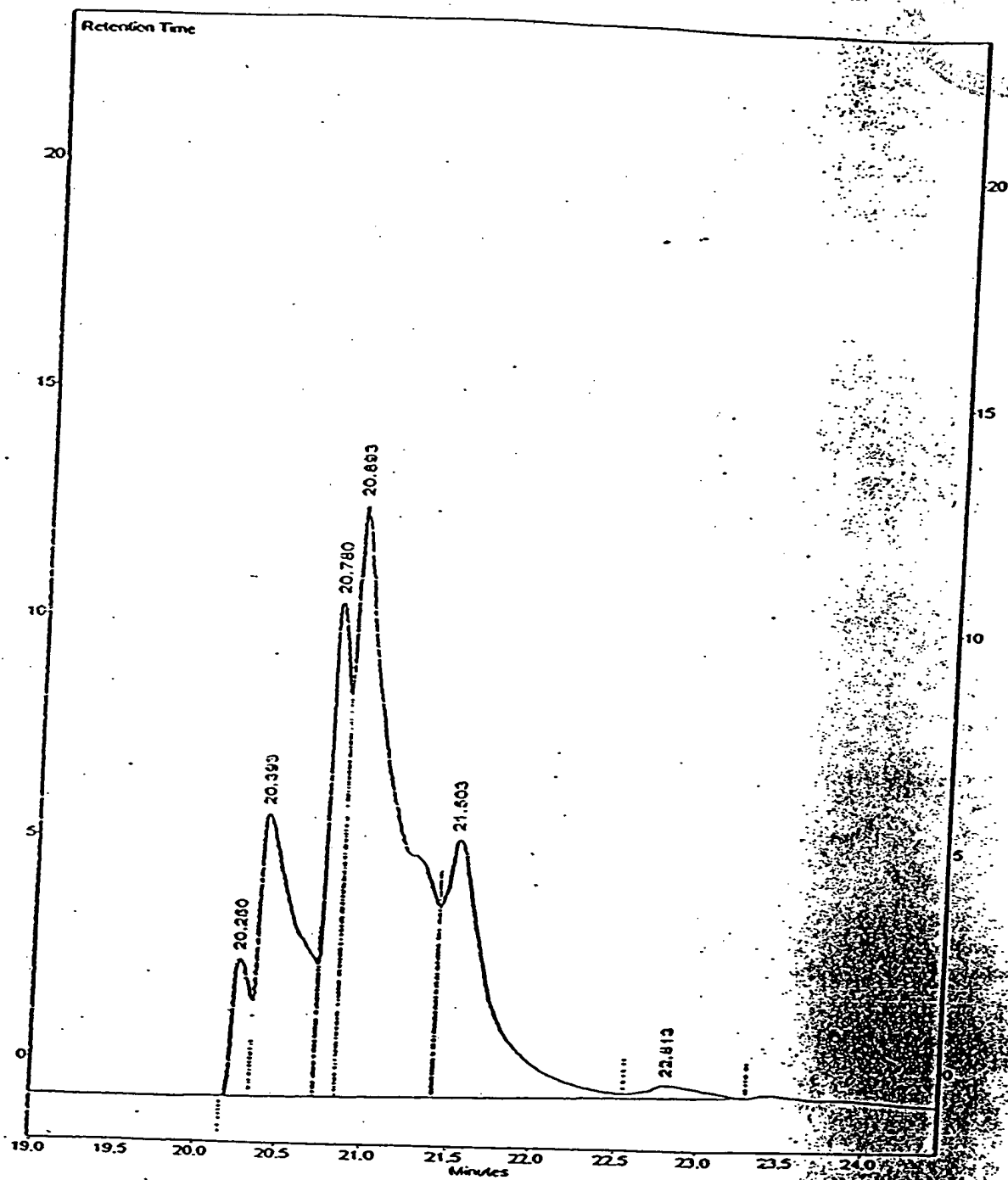


FIG. 17B

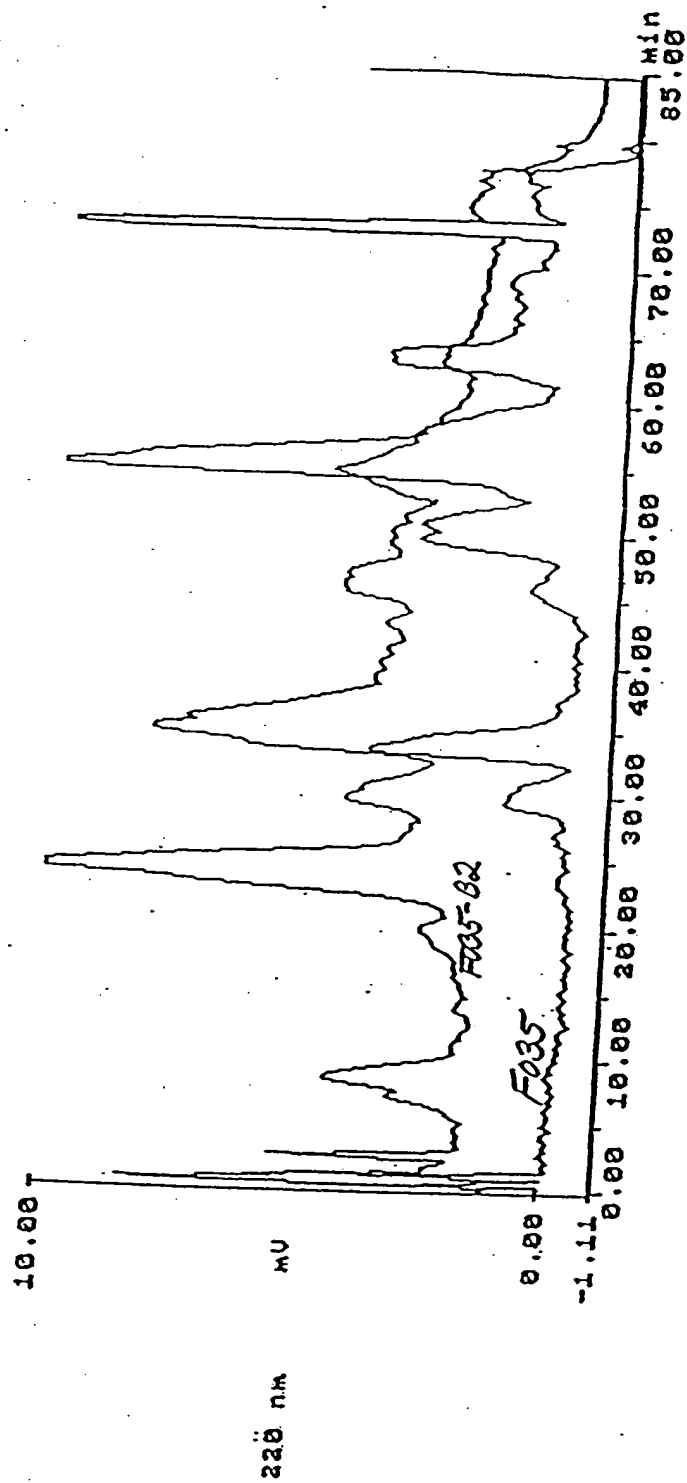


FIG. 18A



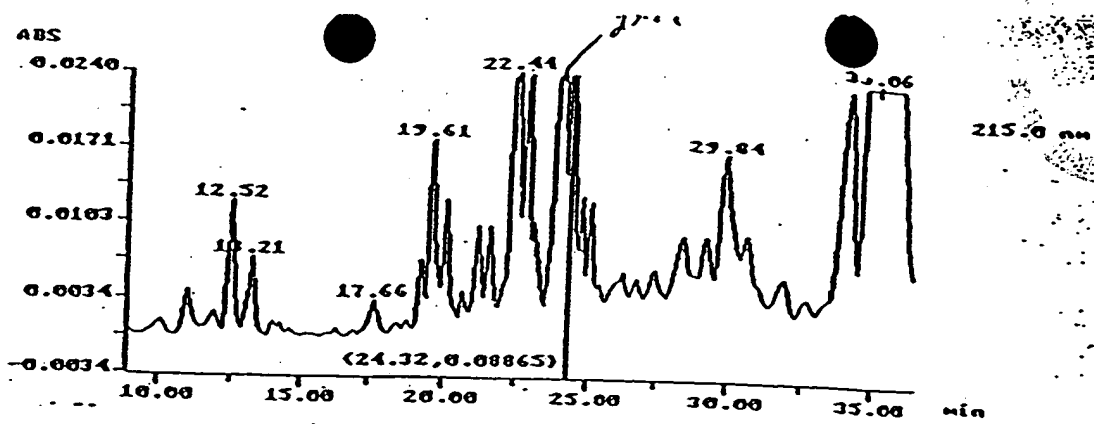


FIG. 18B

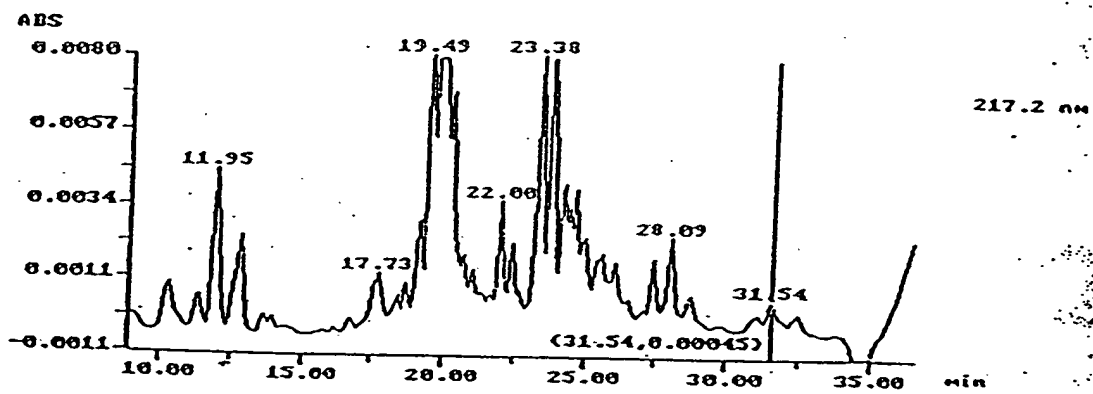


FIG. 18C

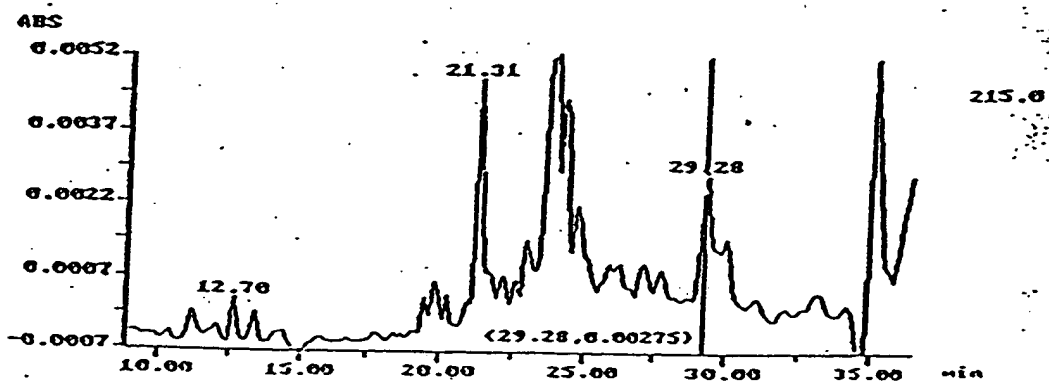


FIG. 18D

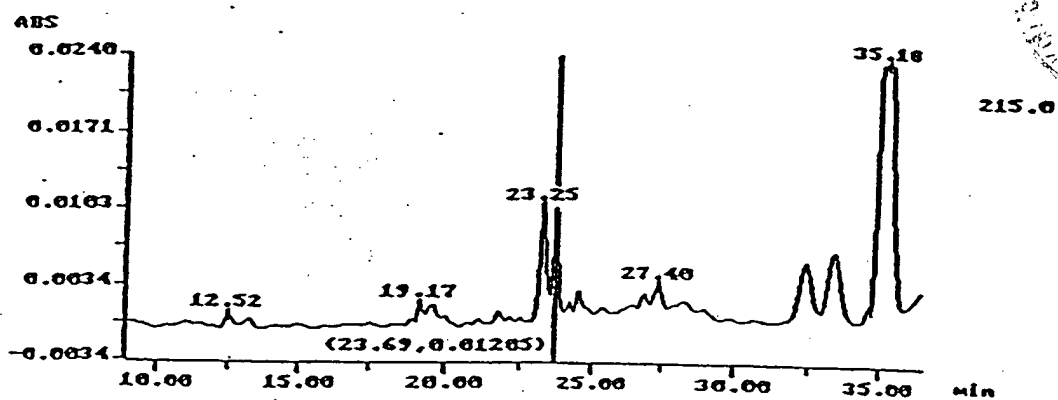


FIG. 18E

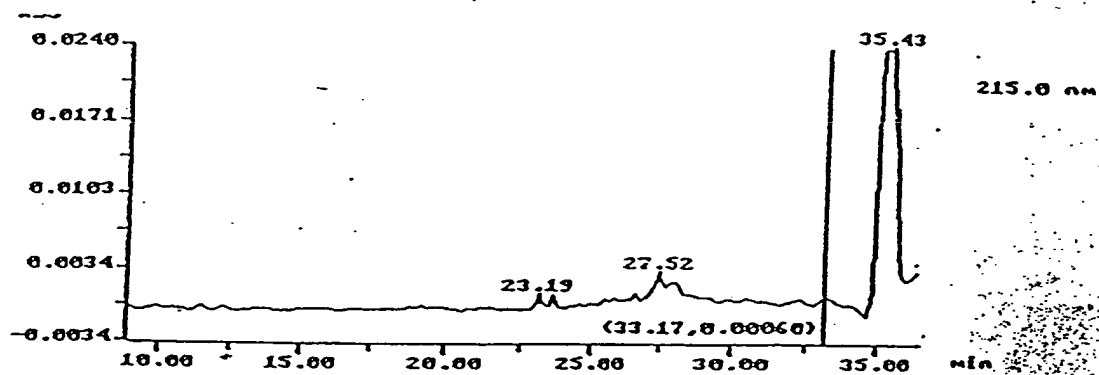


FIG. 18F

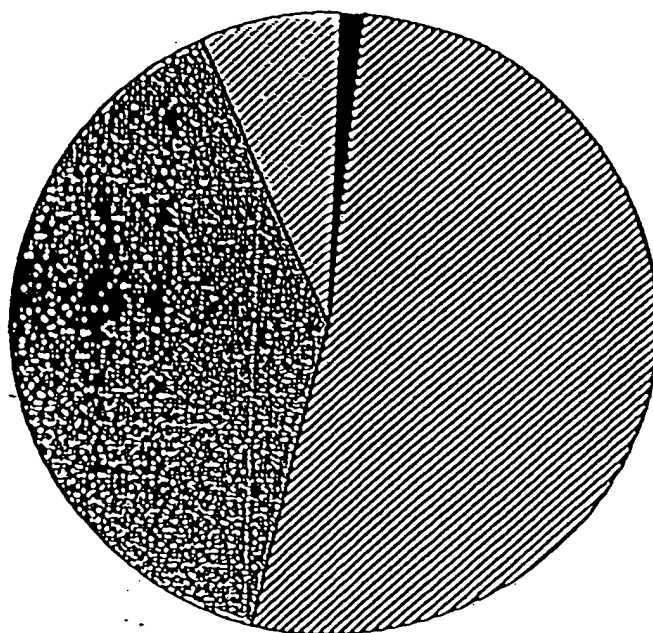


FIG. 19A

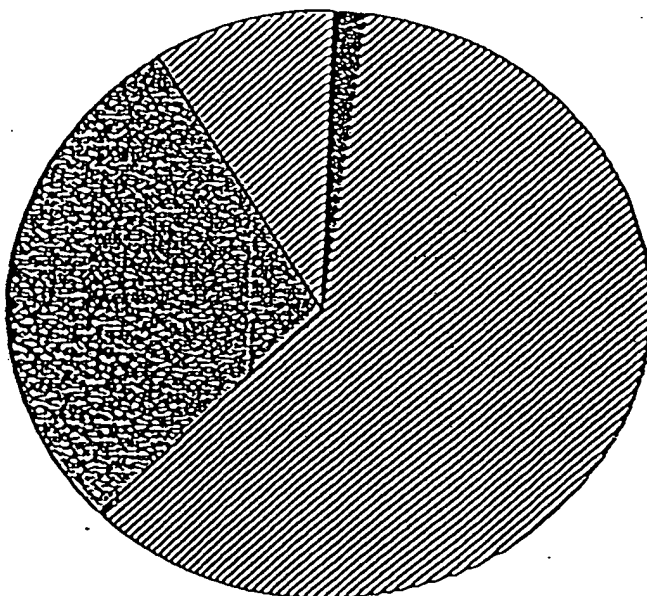


FIG. 19B



- 1 : Untreated
- 2 : TNF (100pM)
- 3 : F035 (1ug/ml)
- 4 : TNF+ F035 (1ug/ml)
- 5 : F035 (2ug/ml)
- 6 : TNF+ F035 (2ug/ml)
- 7 : F094 (1ug/ml)
- 8 : TNF+F094 (1ug/ml)
- 9 : F094 (2ug/ml)
- 10 : TNF+ F094 (2ug/ml)

FIG. 20

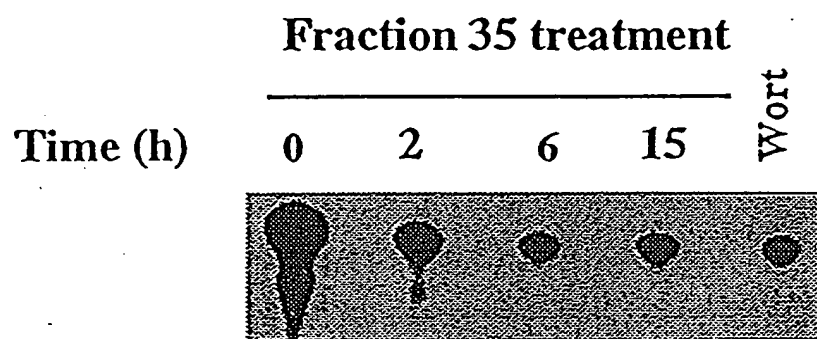


FIG 21

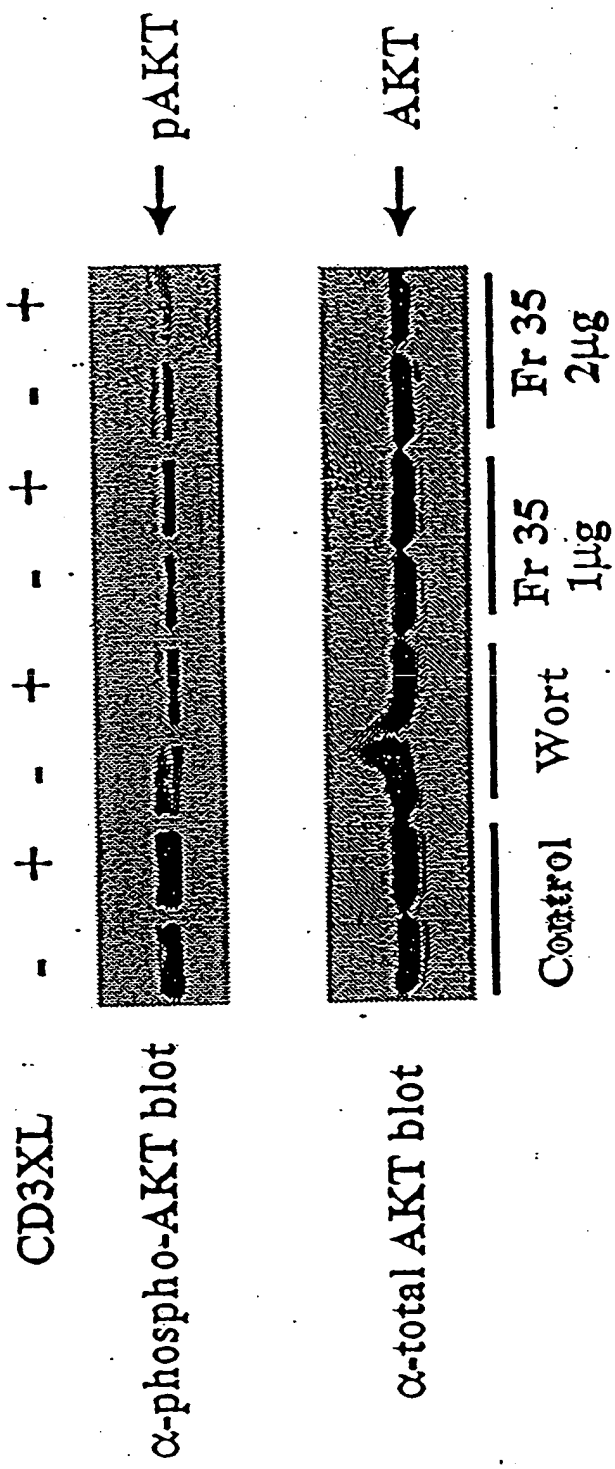


FIG 22



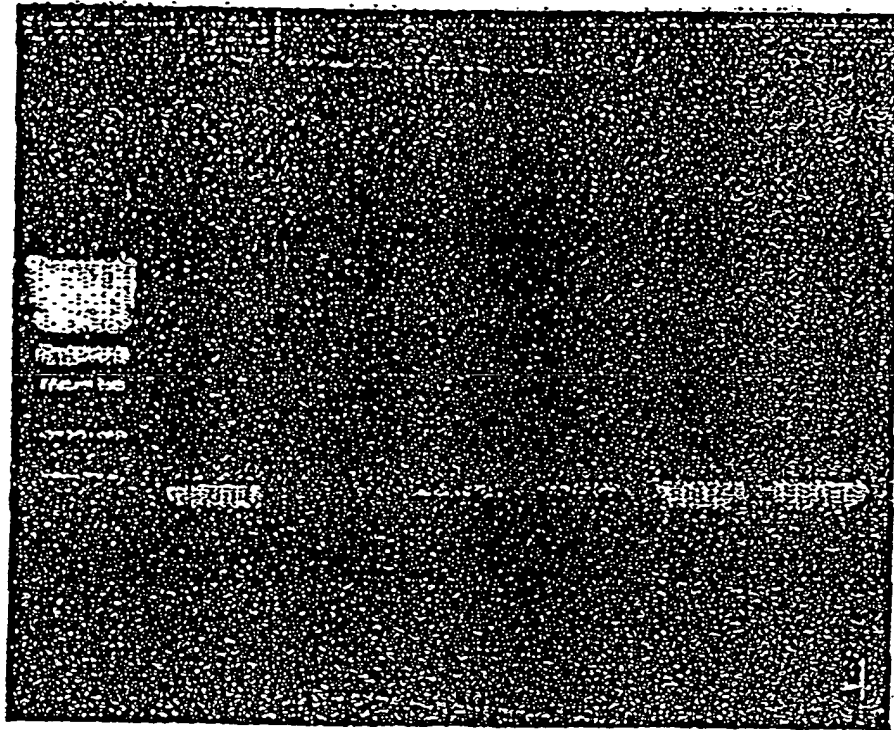


FIG 23

STRUCTURE OF ELLIPTOSIDES:

ELLIPTOSIDE E if R=OH

ELLIPTOSIDE A if R=H

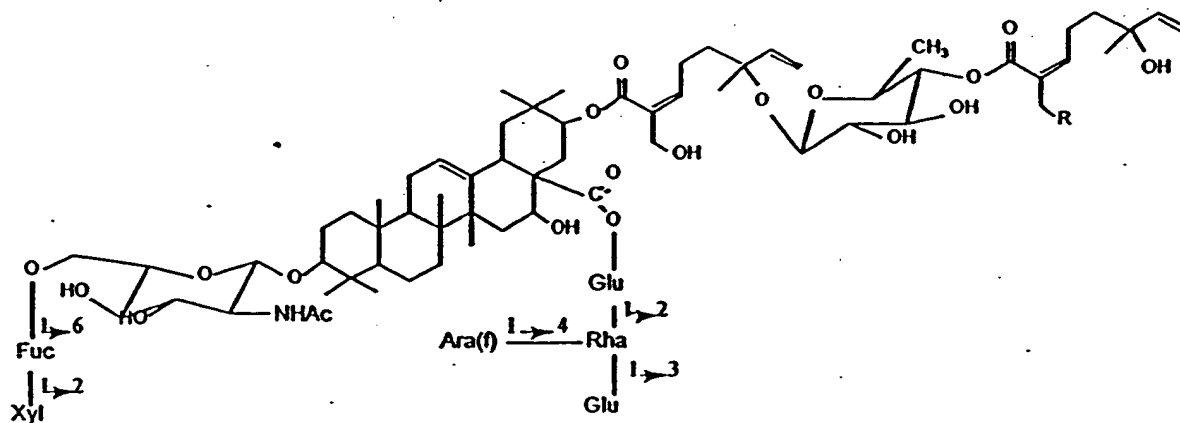
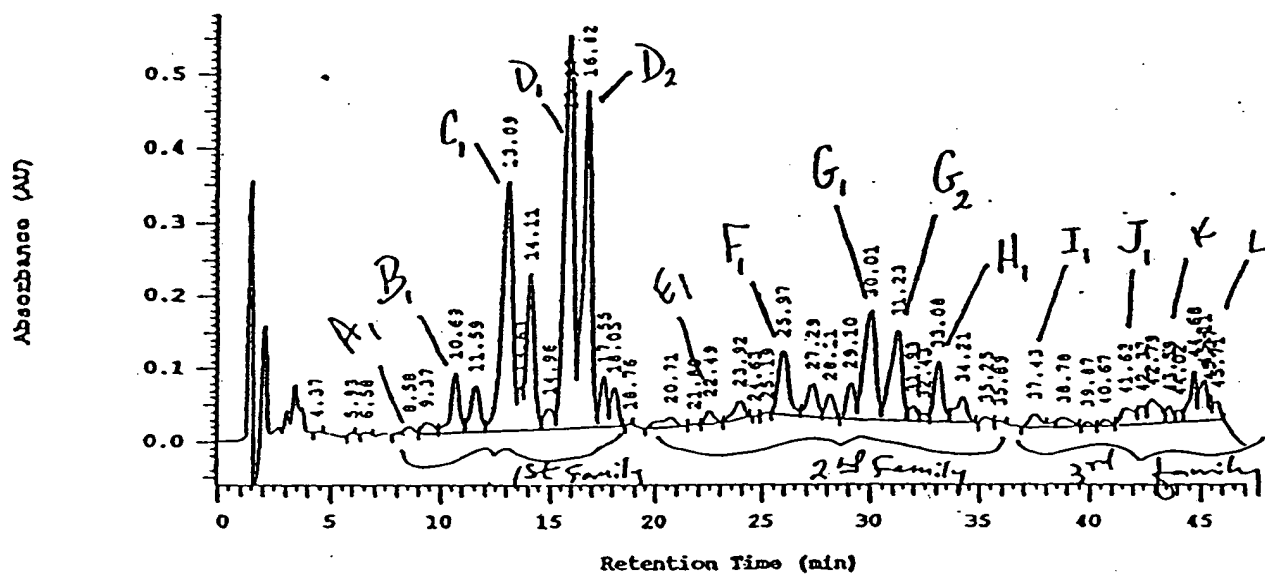
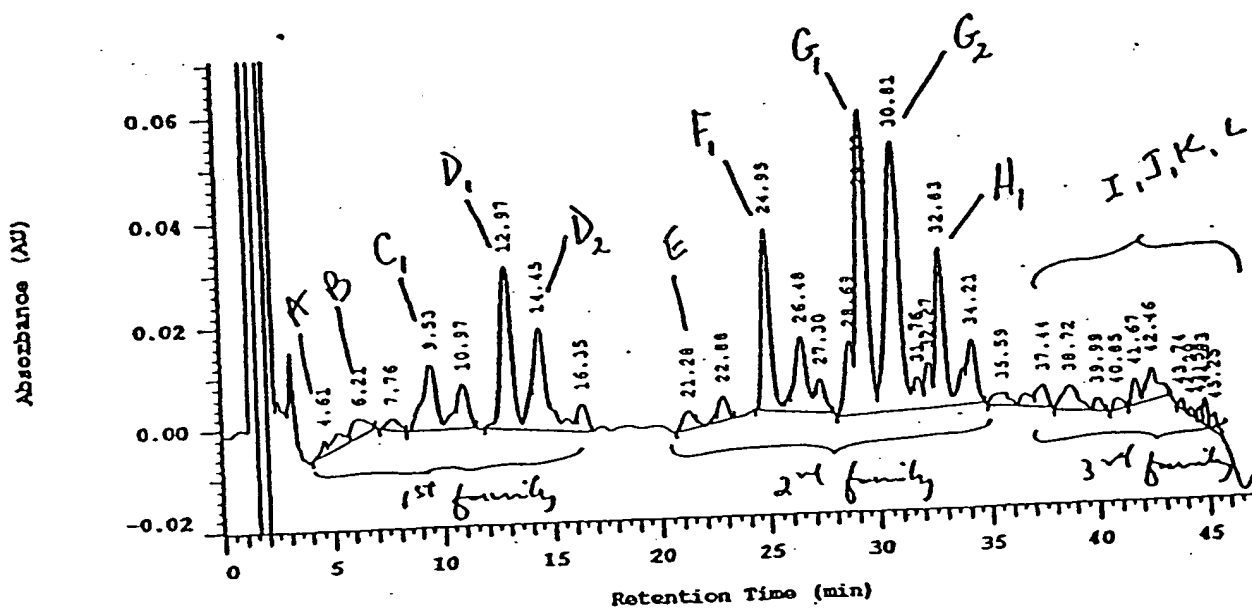


FIG 24



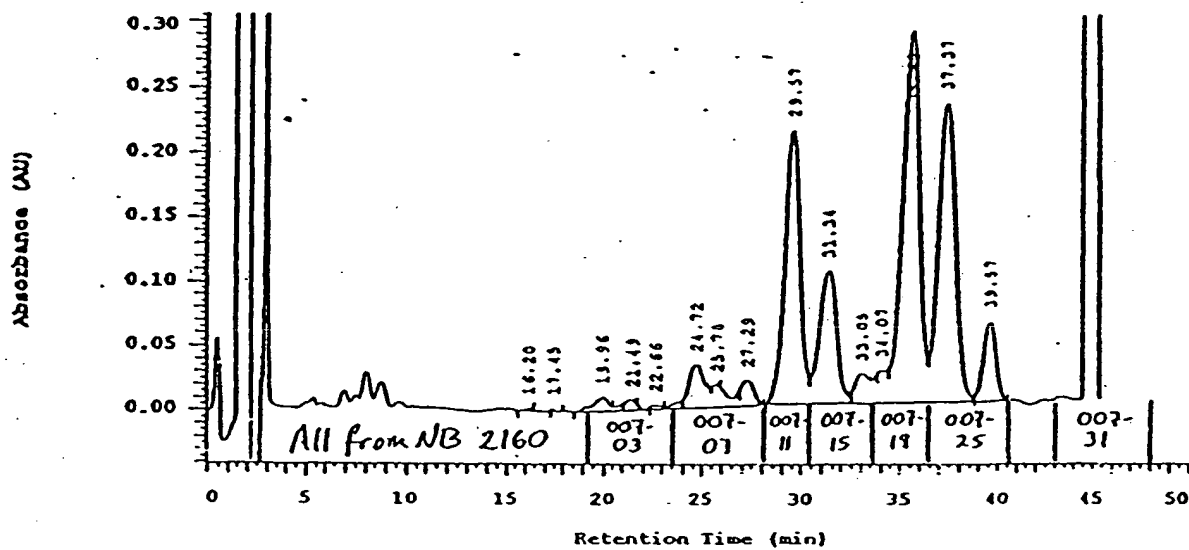
HPLC separation of the constituents in F094

FIG 25



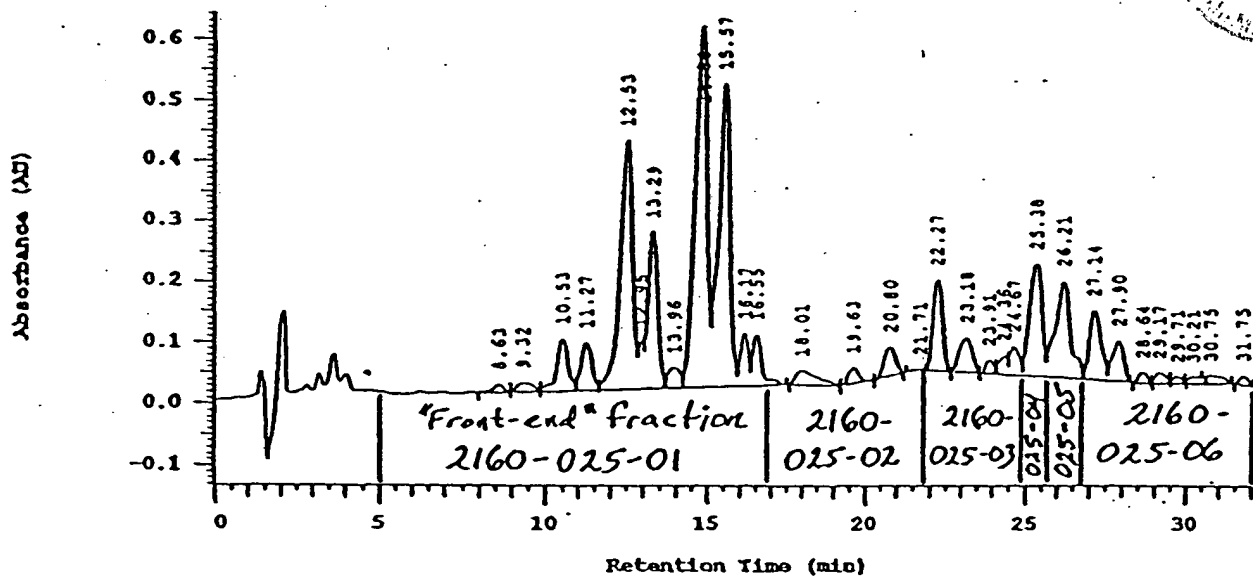
HPLC separation of the constituents in F035

FIG 26



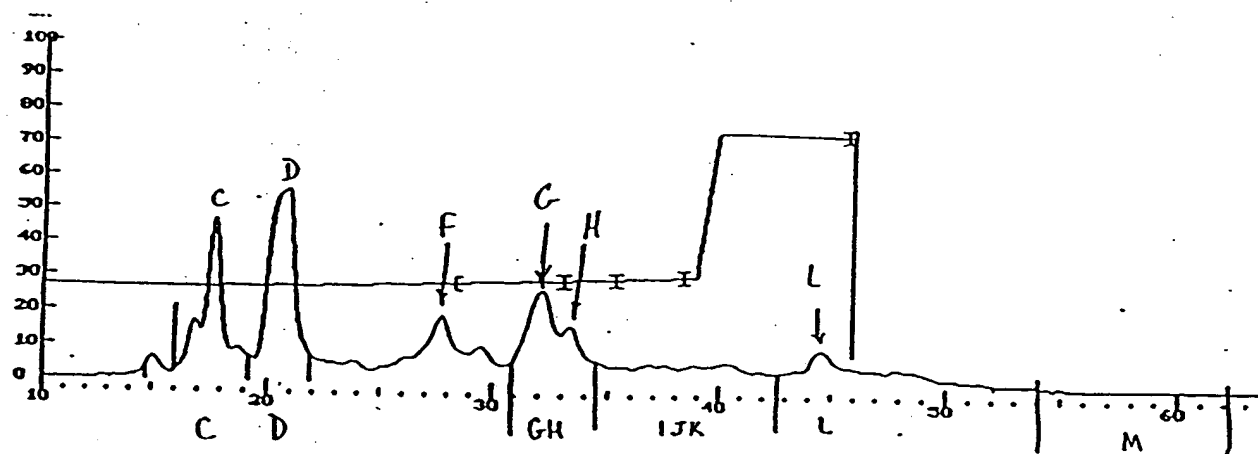
First Fractionation by Semi-Prep HPLC of F094

FIG 27



Second Fractionation by Semi-Prep HPLC of F094

FIG 28



Prep Fractionation of F094

FIG 29

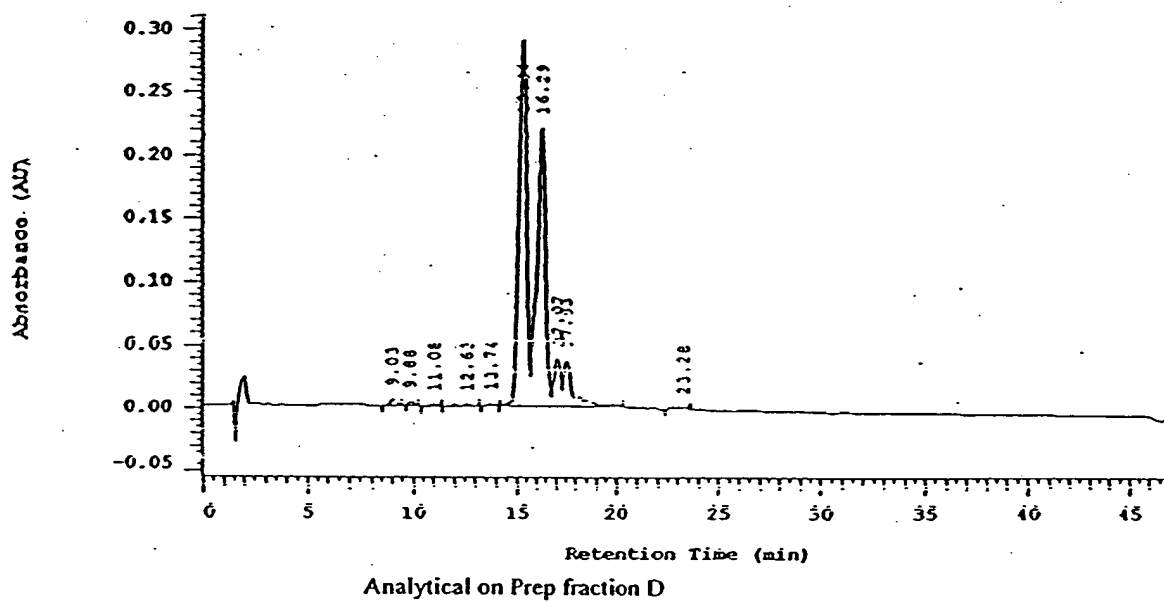


FIG 30

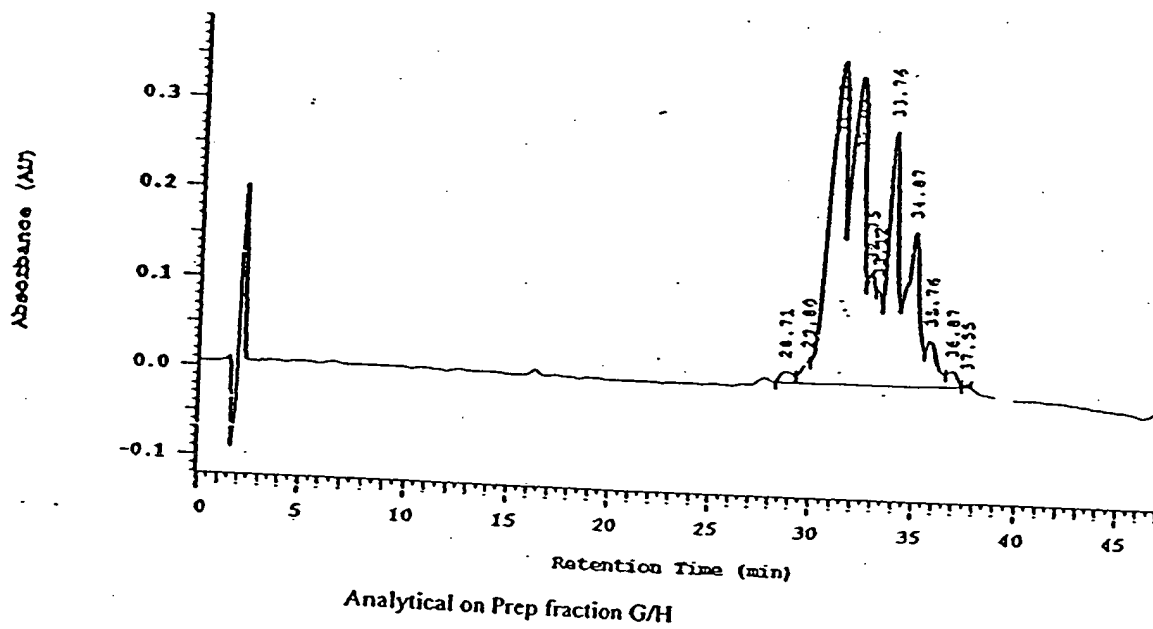
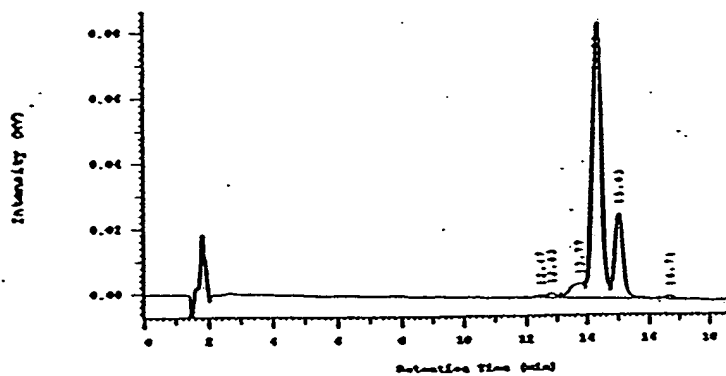
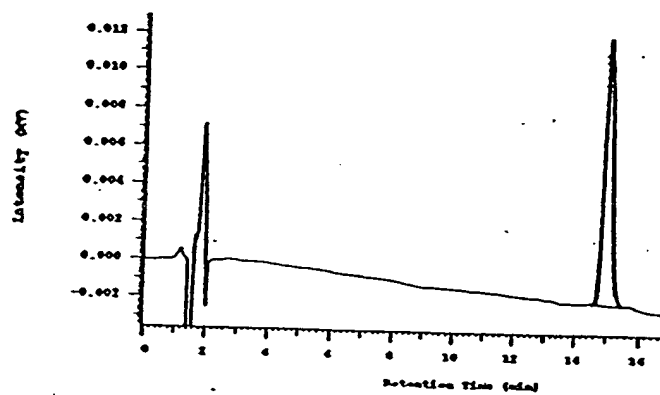


FIG 31



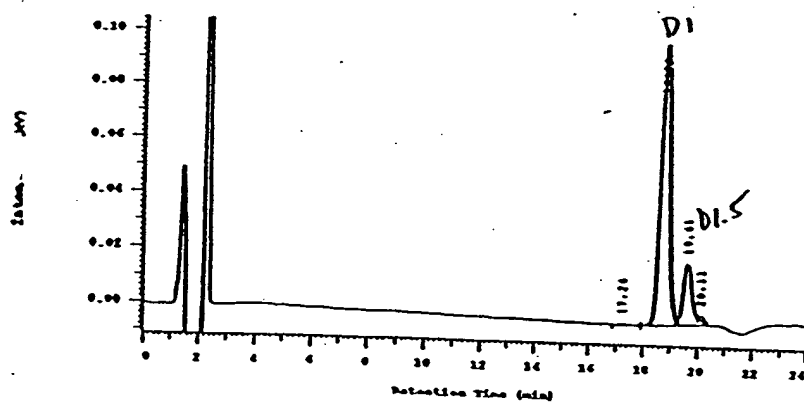
GI after second PFP column purification.

FIG 32



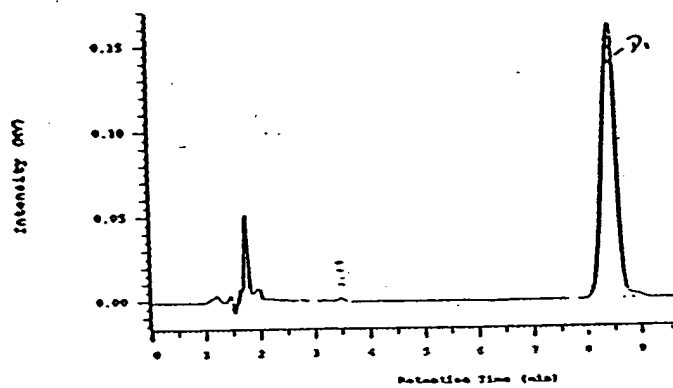
GI after final C-18 purification

FIG 33



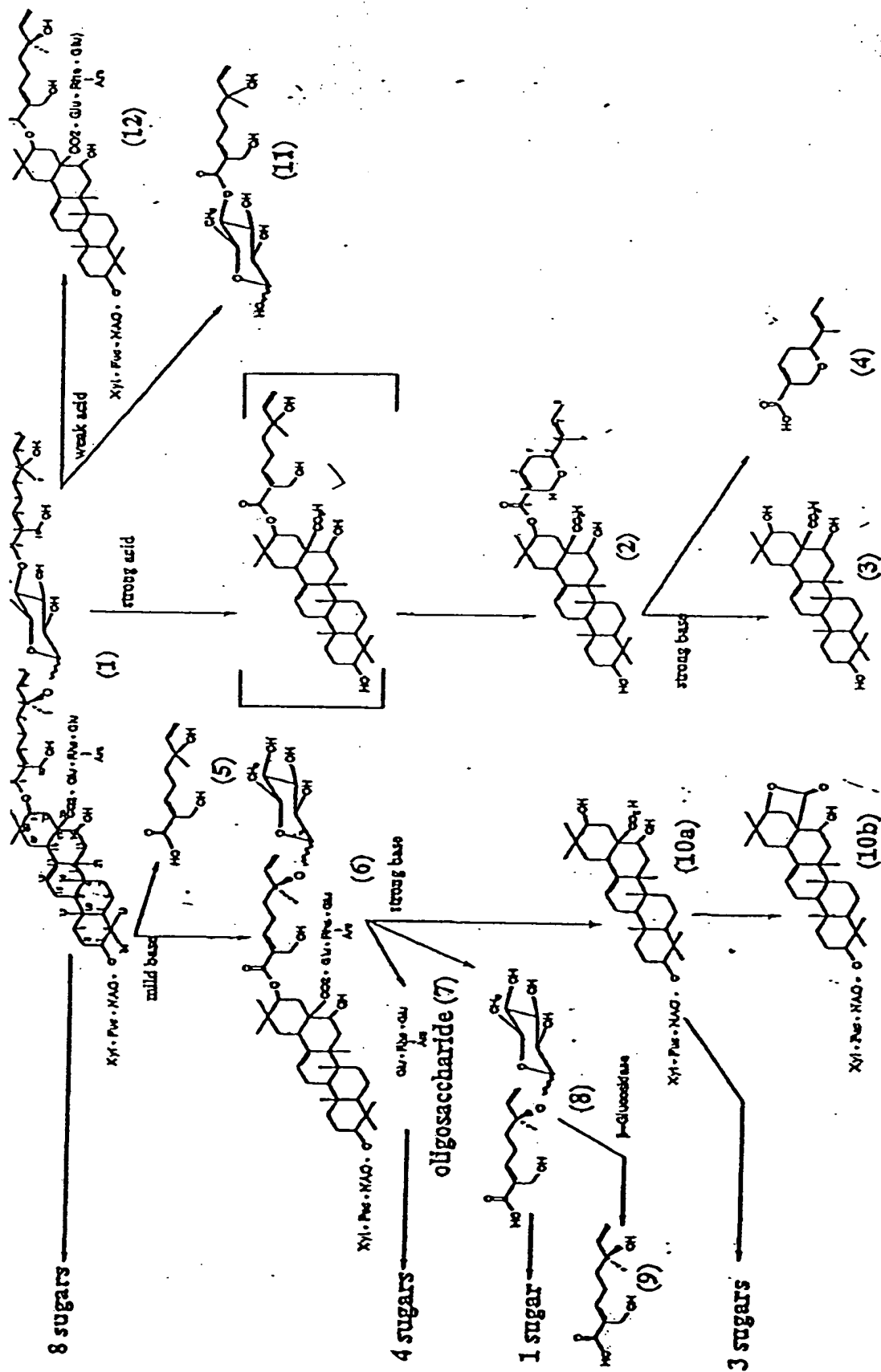
D1 after Waters C-18 column purification.

FIG 34



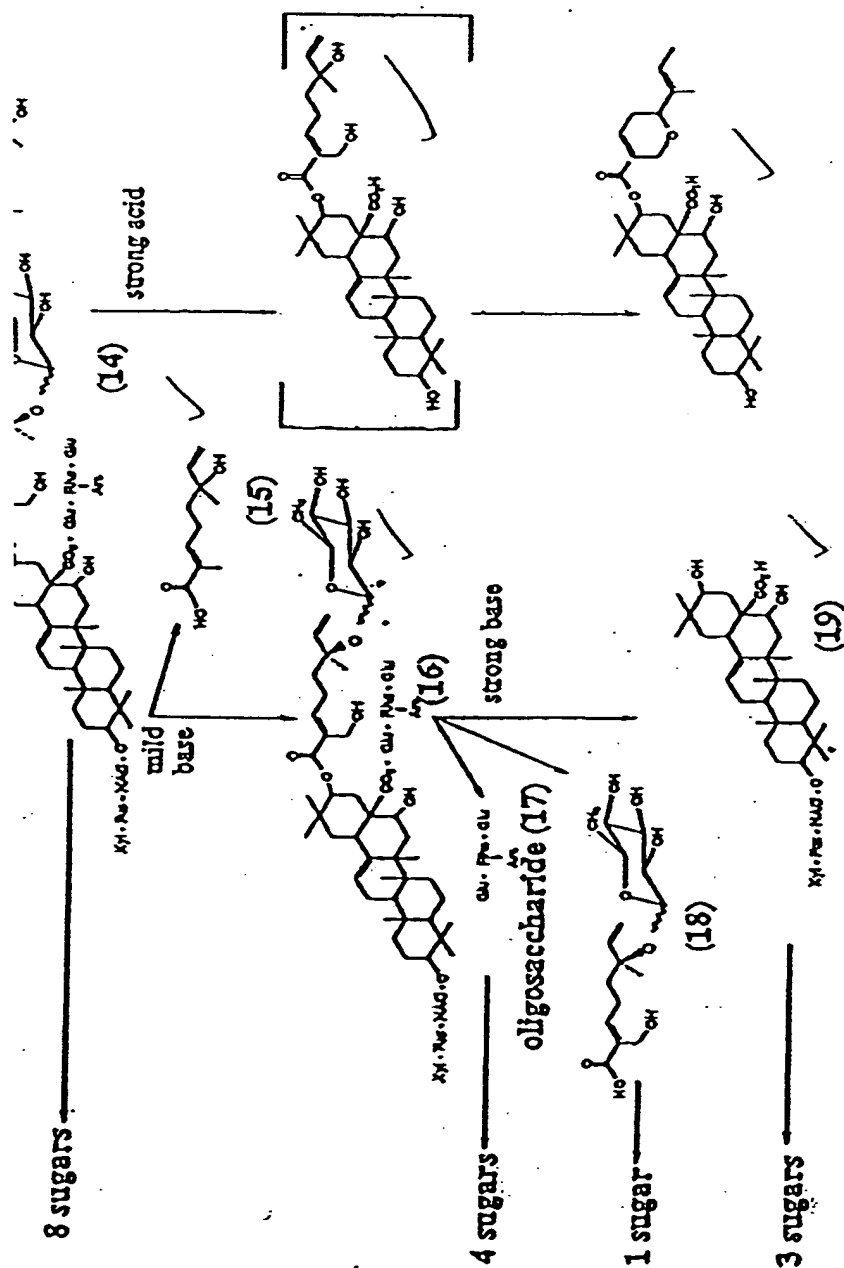
DI after final C18-Aq purification

FIG 35

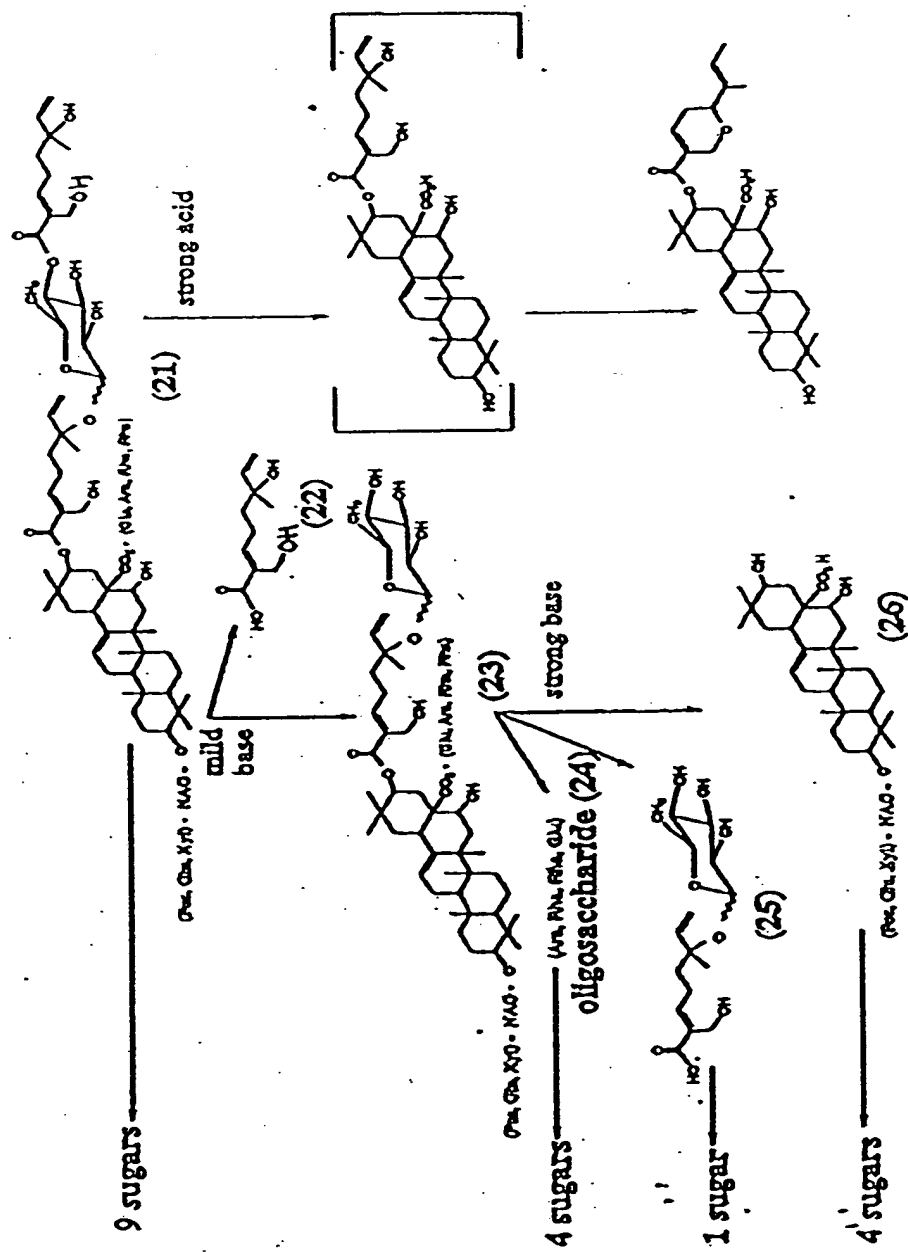


Compounds from the Degradation of D1

FIG 36



Compounds from the Degradation of G1



Compounds from the Degradation of B1

FIG. 38

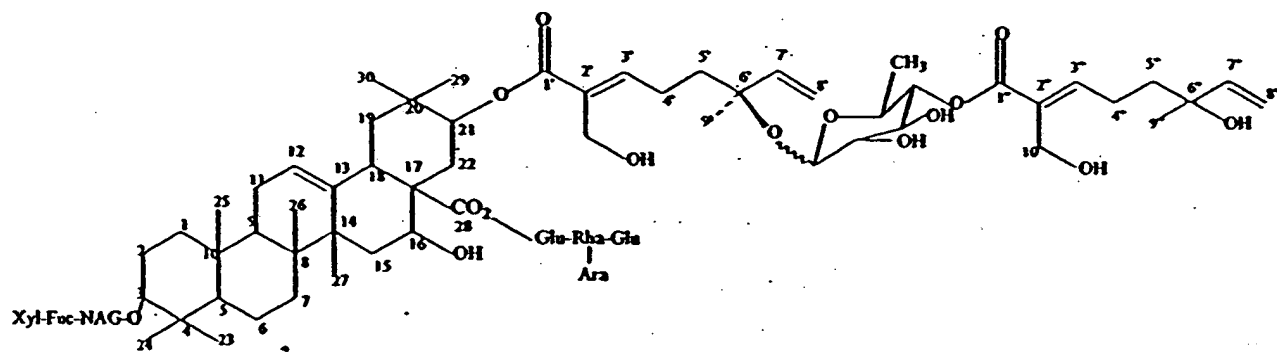


FIG. 39

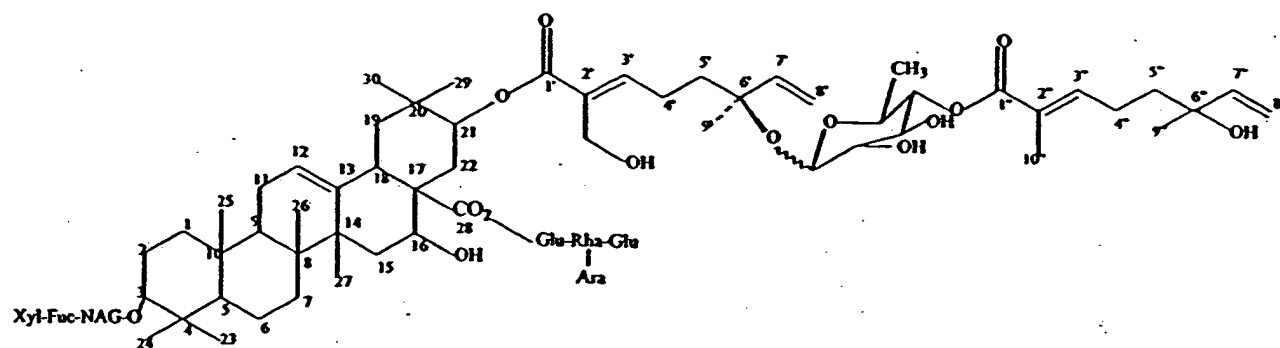


FIG. 40

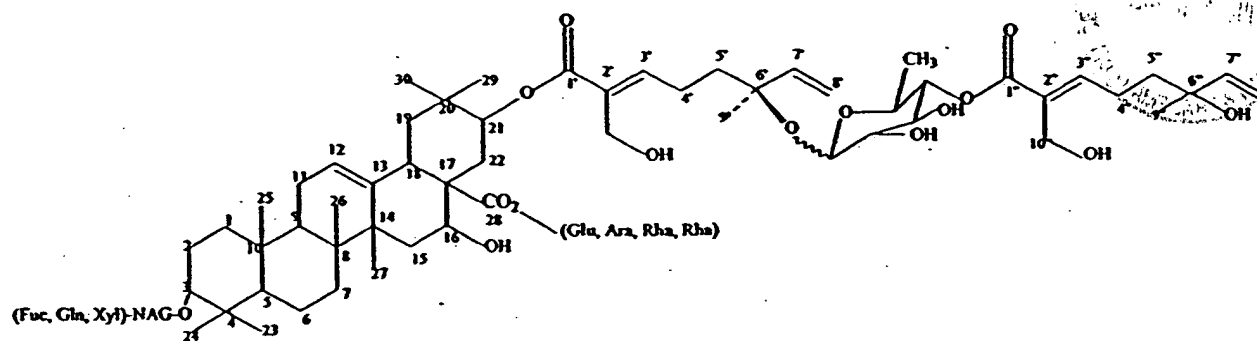
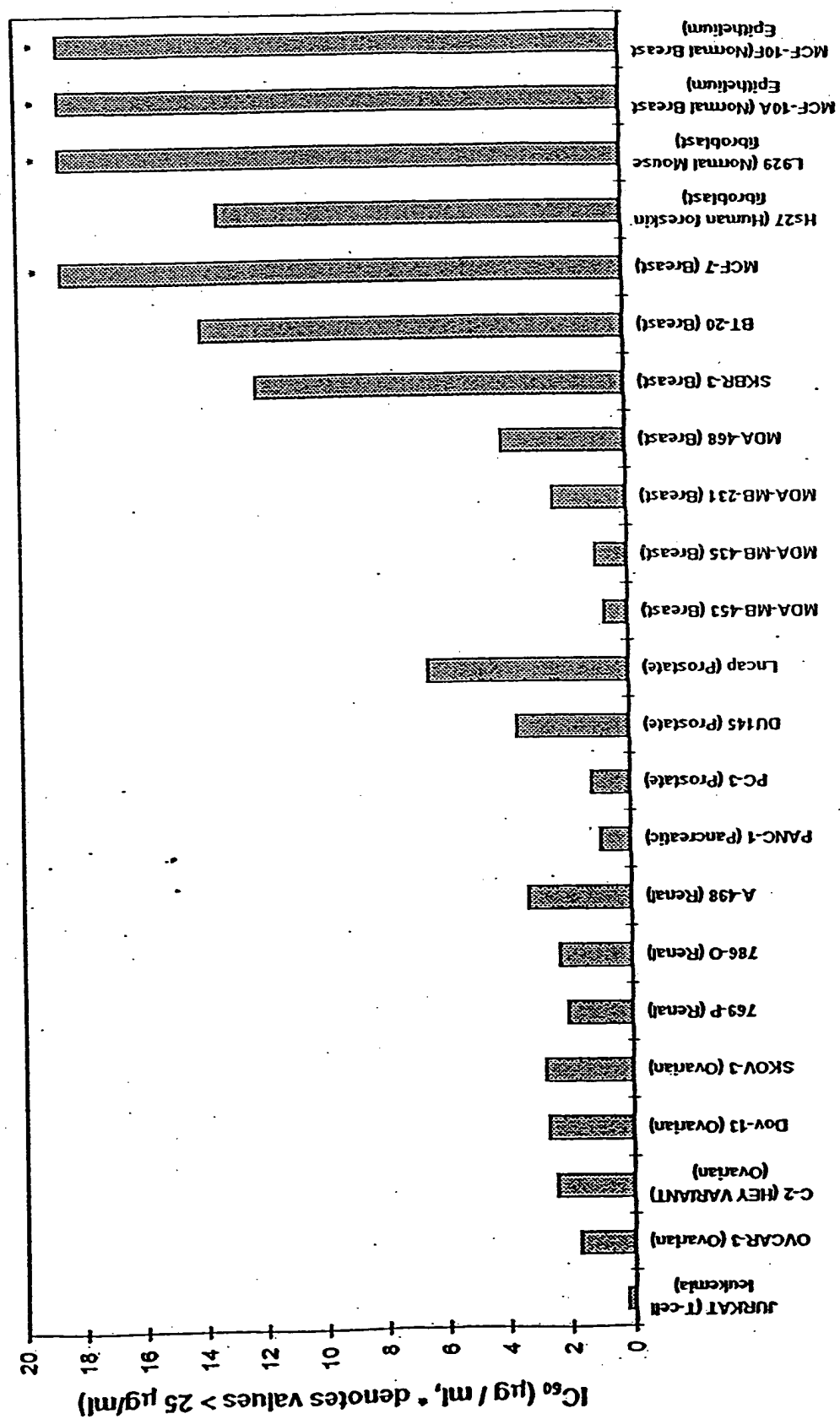


FIG. 41



Cell Lines

FIG. 42

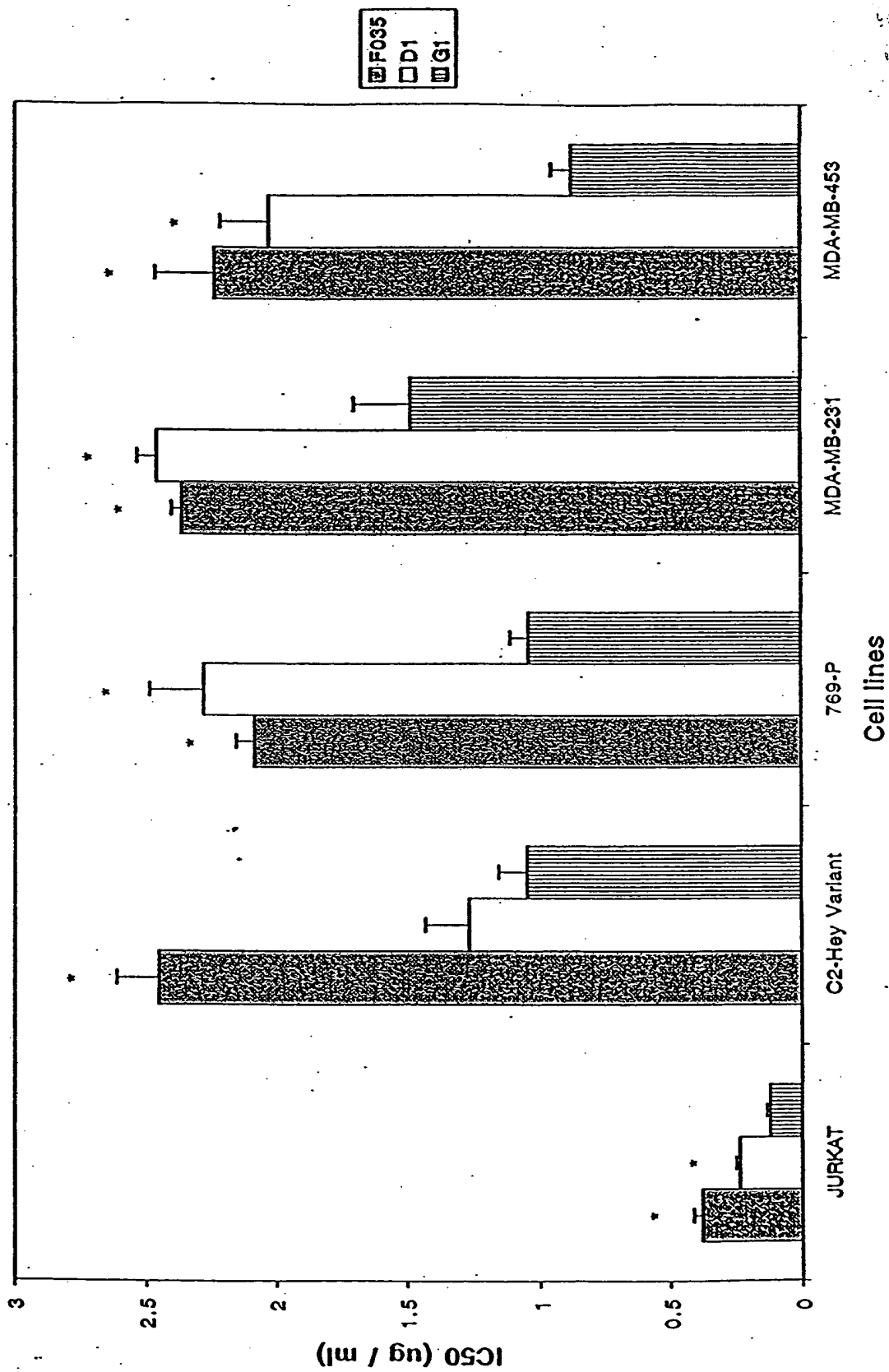
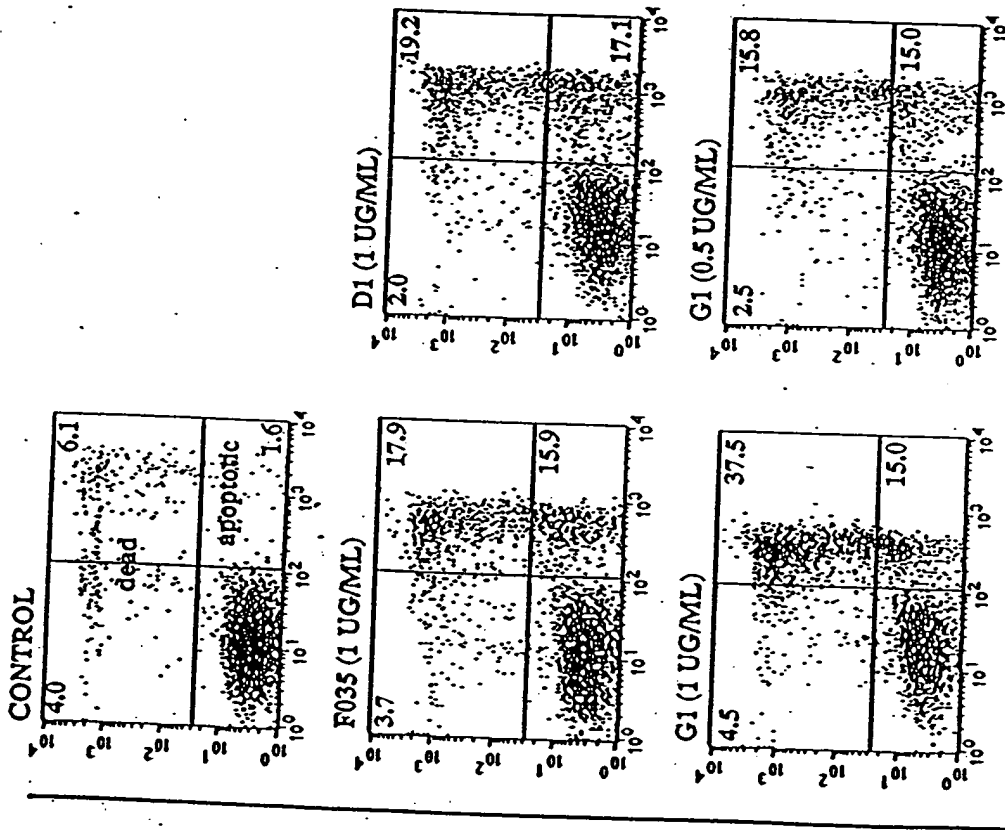


FIG 43





ANNEXIN-V-FITC

FIG 44

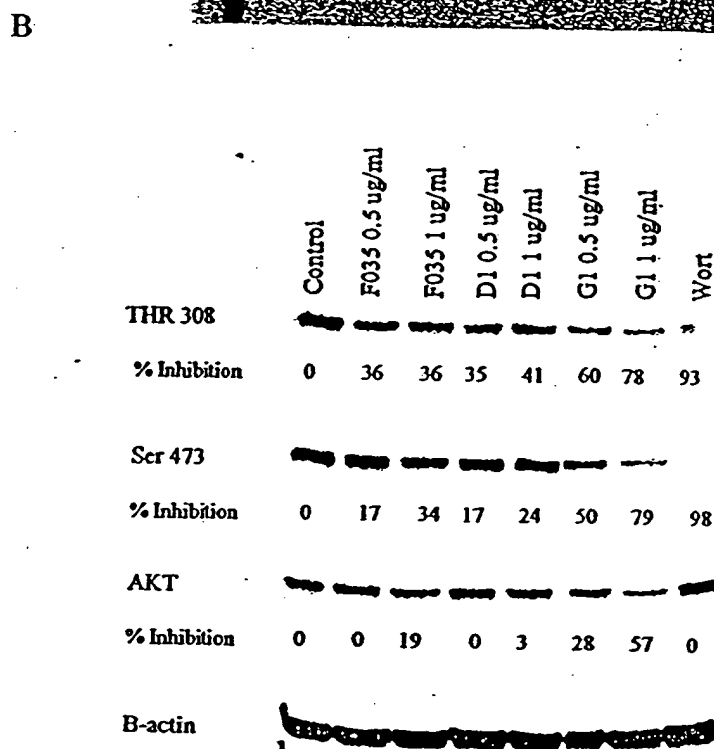
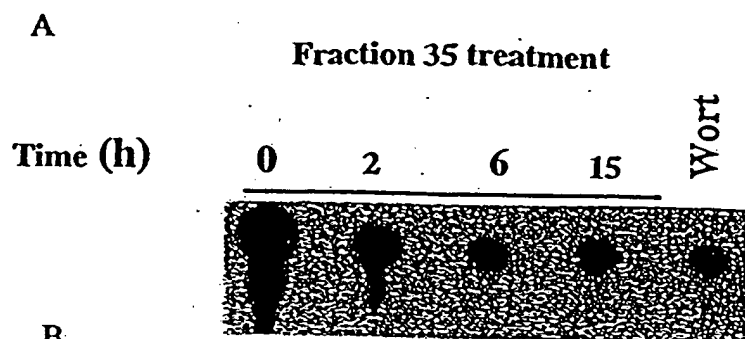
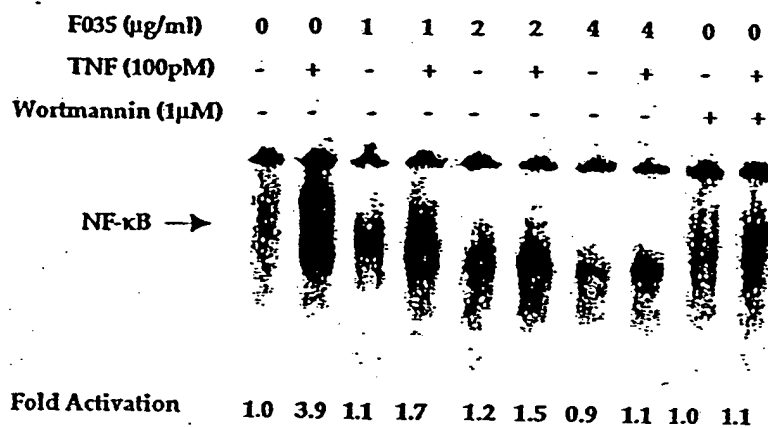
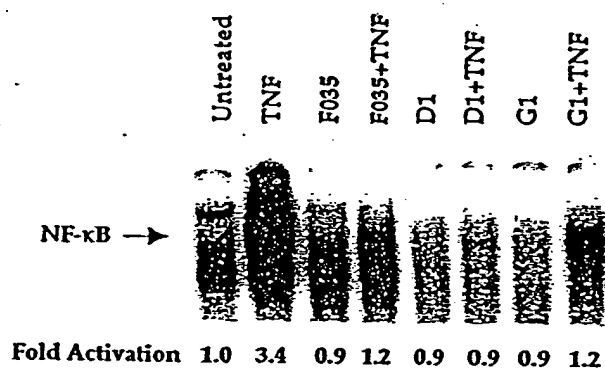


FIG 45

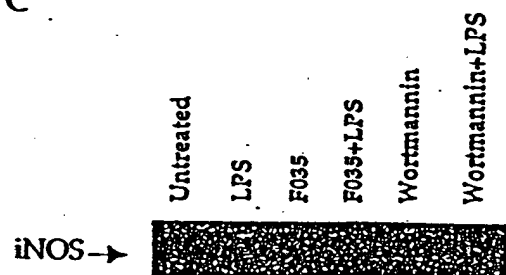
A



B



C



D

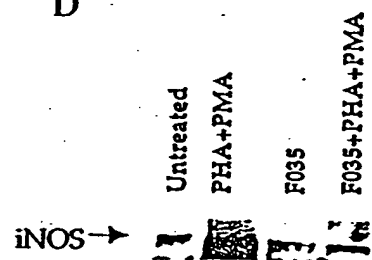
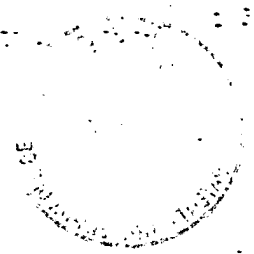


FIG 46



Effect of F035 & D1 on cleavage of PARP in Jurkat cells.

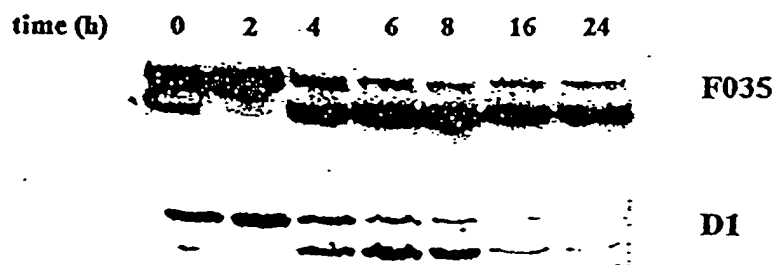


FIG 47



Effect of z-vad fmk on F035 induced PARP cleavage in Jurkat cells

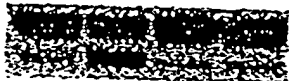
F035	-	+	-	+
z-vad fmk	-	-	+	+
				

FIG 48



Effect of F035, F094, D1 & G1 on caspase activity in Jurkat cells.

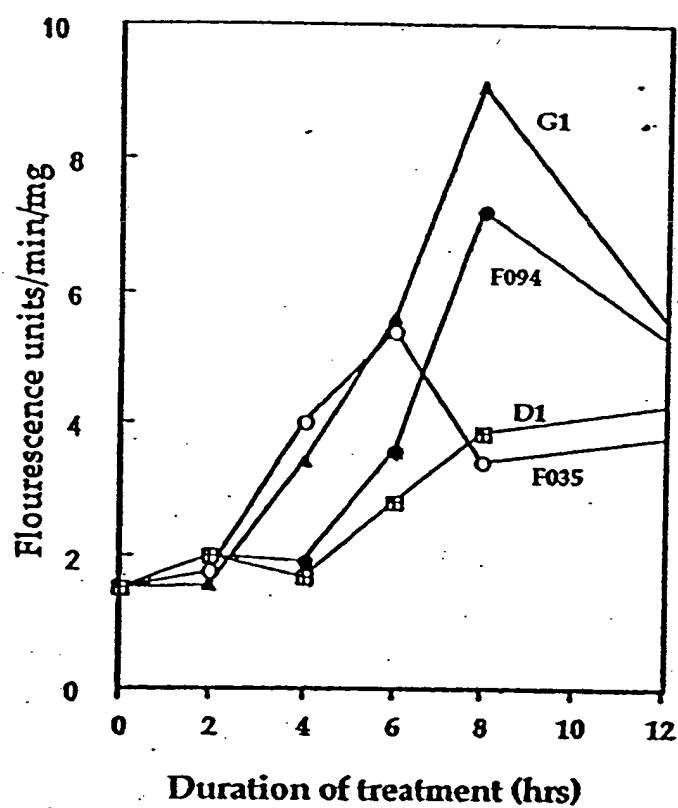


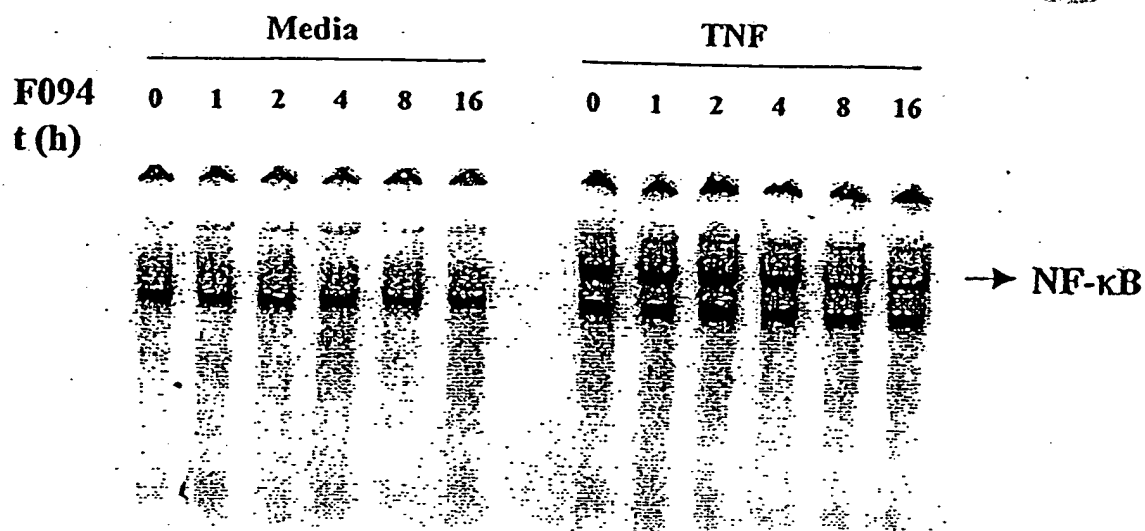
FIG 49

Effect of F035 on cytochrome c release from Jurkat mitochondria

time (h) 0 4 6
 → Cytochrome c

FIG 50

A



B

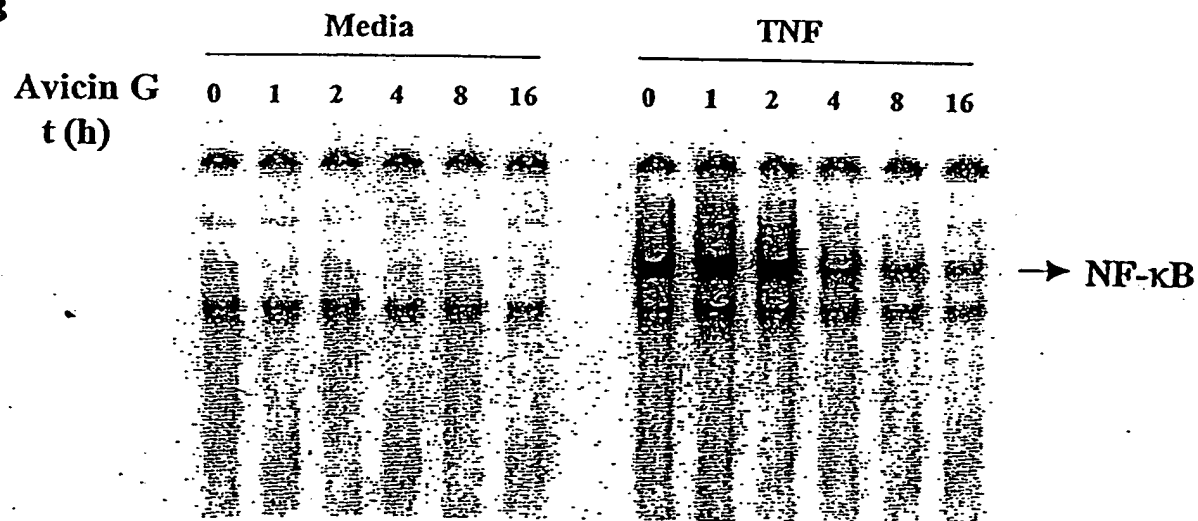
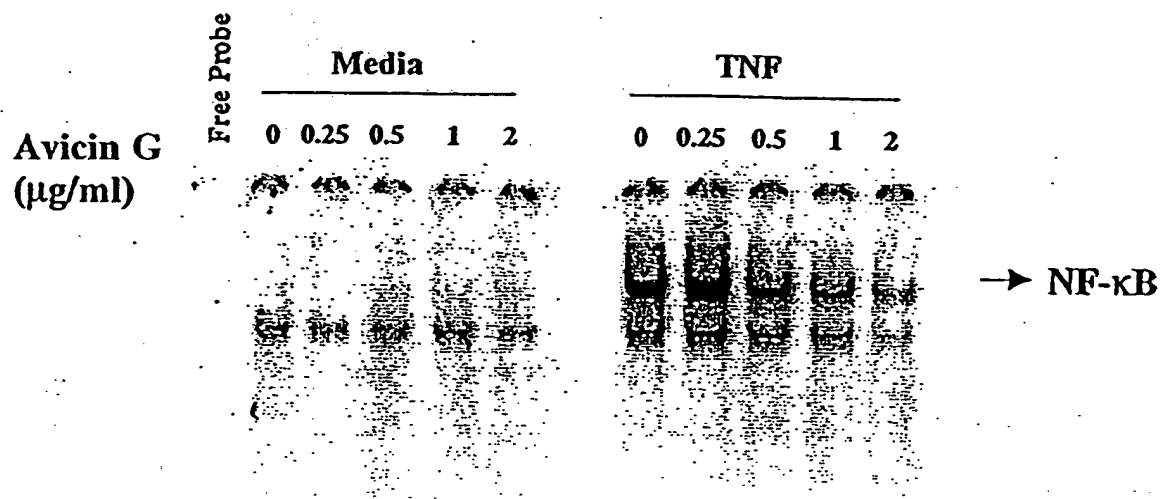


FIG. 51 A-B



A



B

Rabbit IgG	-	-	-	-	-	+
anti-p65	-	-	-	-	+	-
Cold wt	-	-	-	+	-	-
Cold mut	-	-	+	-	-	-
TNF	-	+	+	+	+	+

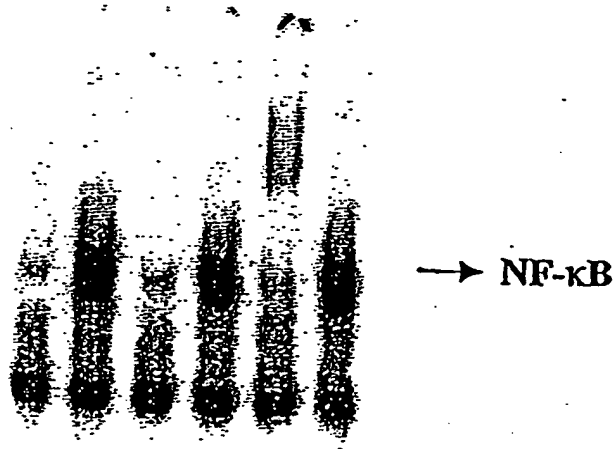
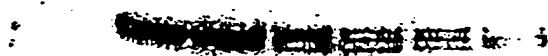


FIG. 52 A-B



A **I κ B**

Time (min) 0 2 5 10 15 30



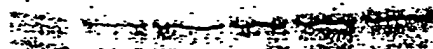
Untreated



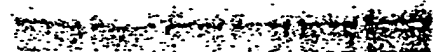
Avicin G

B **p65**

Time (min) 0 2 5 10 15 30



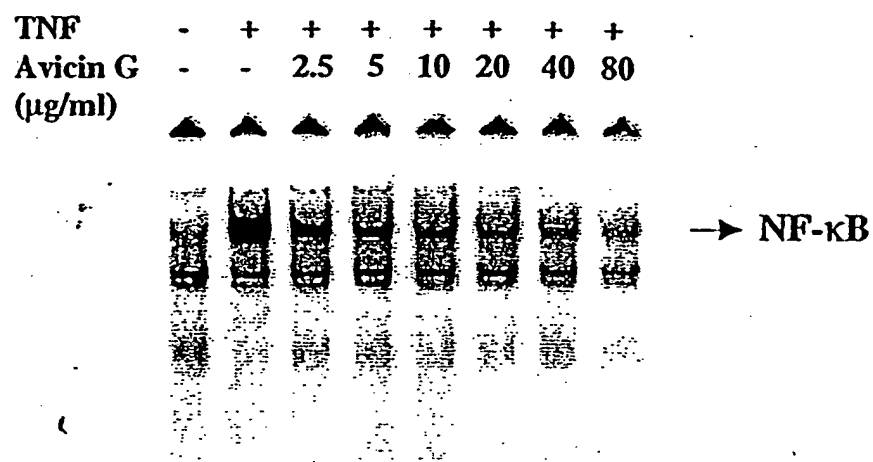
Untreated



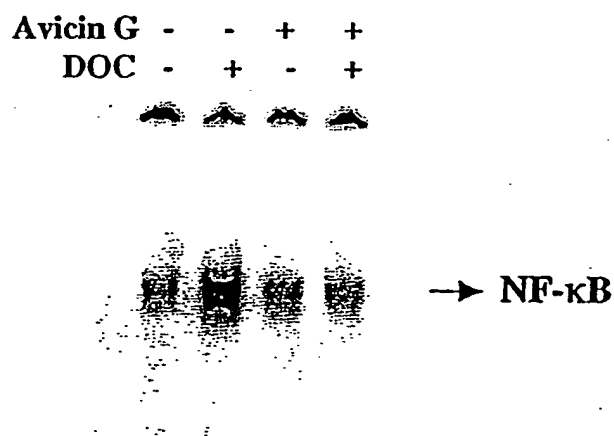
Avicin G

FIG. 53 A-B

A



B



C

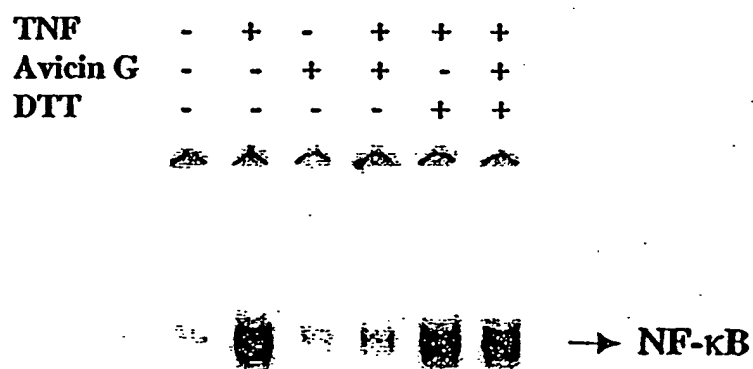
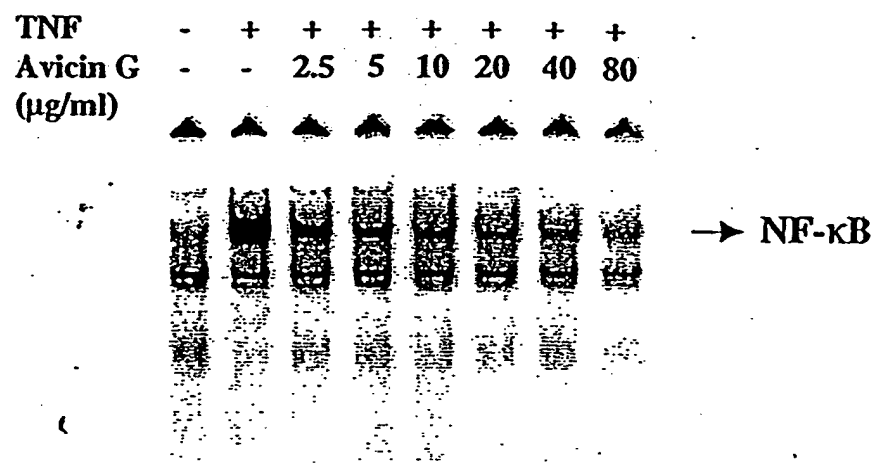
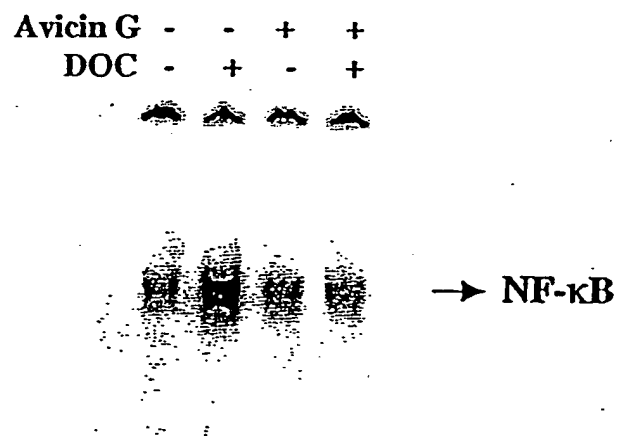


FIG. 54 A, B, C

A



B



C

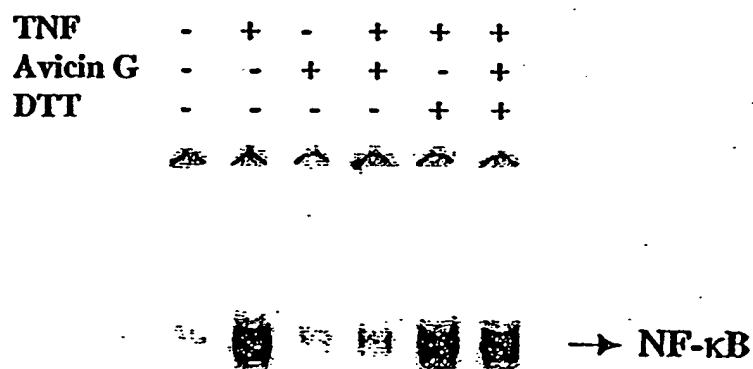
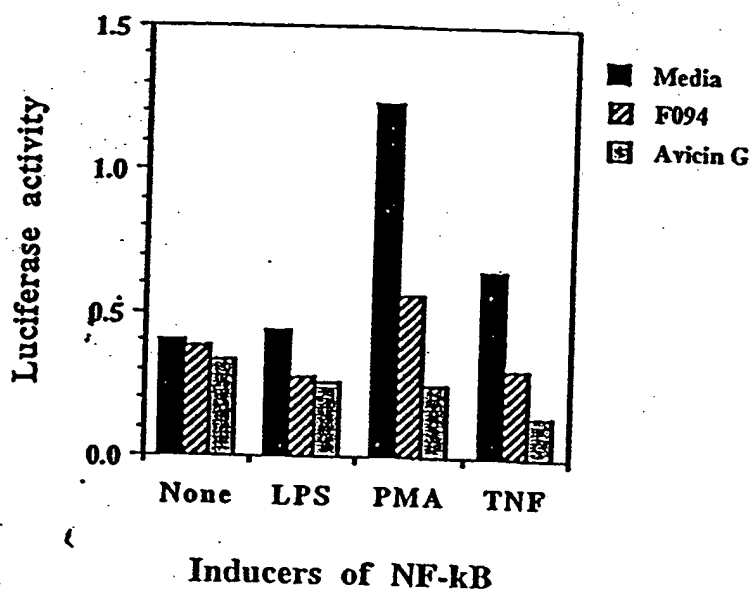


FIG. 54 A, B, C

A



B

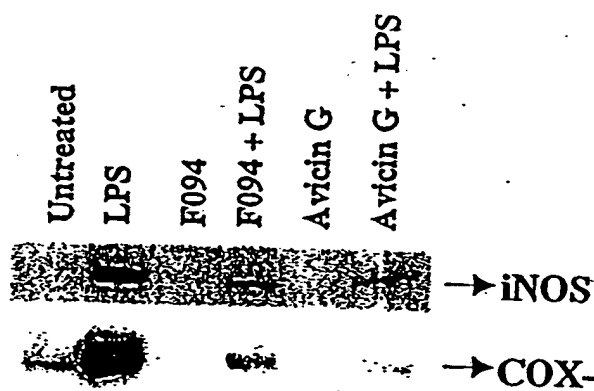
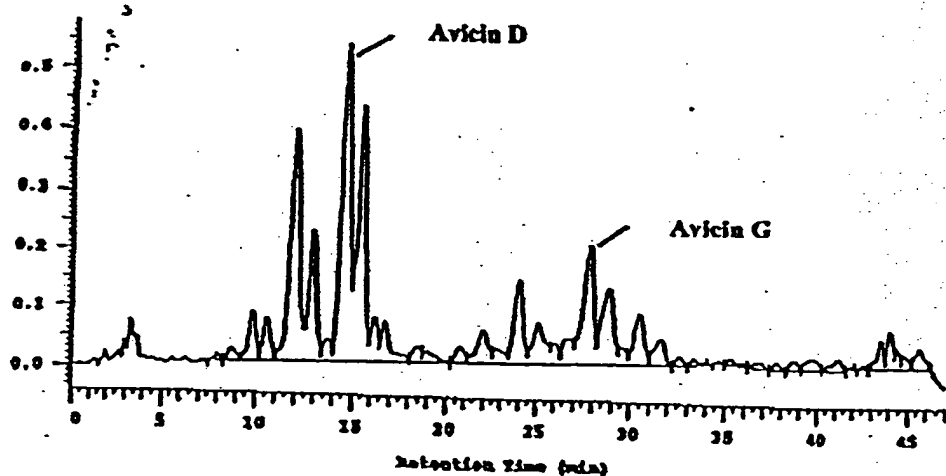


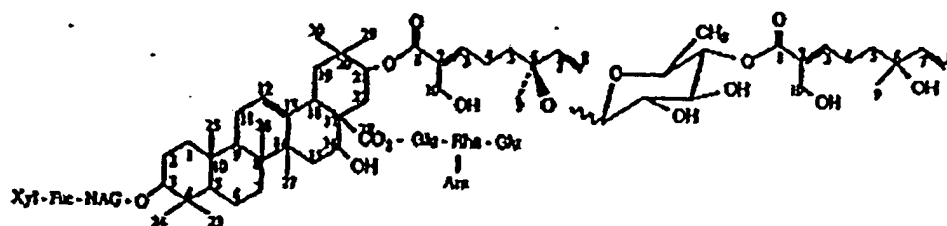
FIG. 55 A, B



IC₅₀ Values

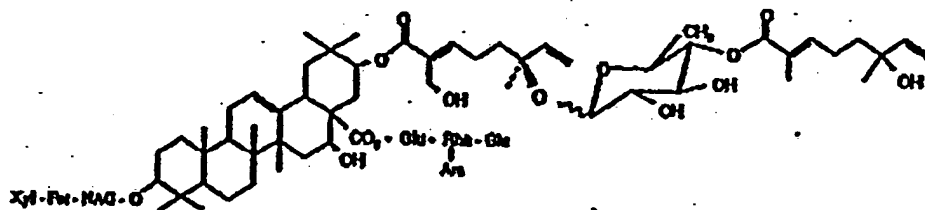
HPLC Separation of the Avicins in F094

0.331-0.407 $\mu\text{g/ml}$



Avicin D

0.320-0.326 $\mu\text{g/ml}$



Avicin G

0.160-0.181 $\mu\text{g/ml}$

Annexin-V positive cells (%)

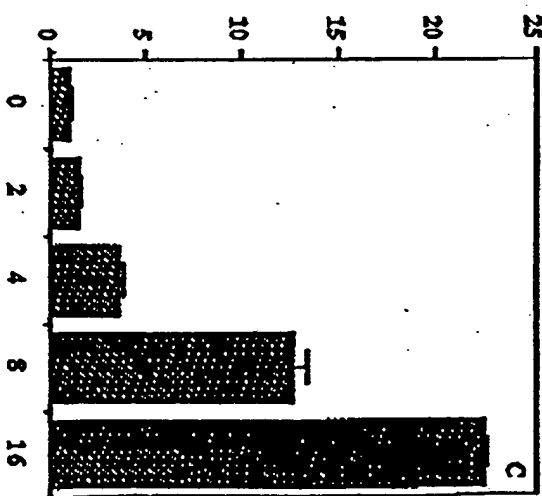
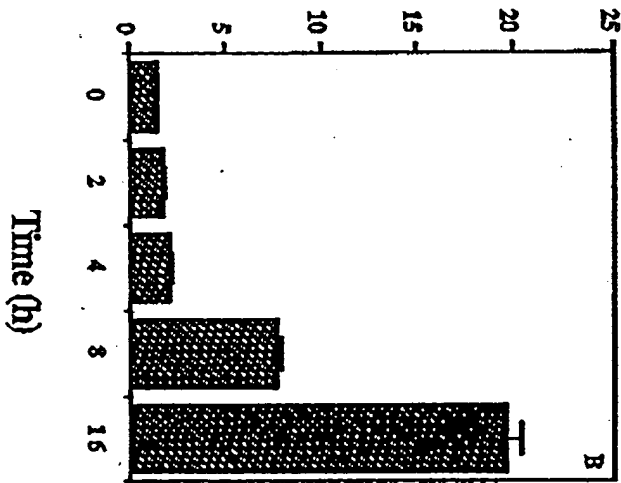
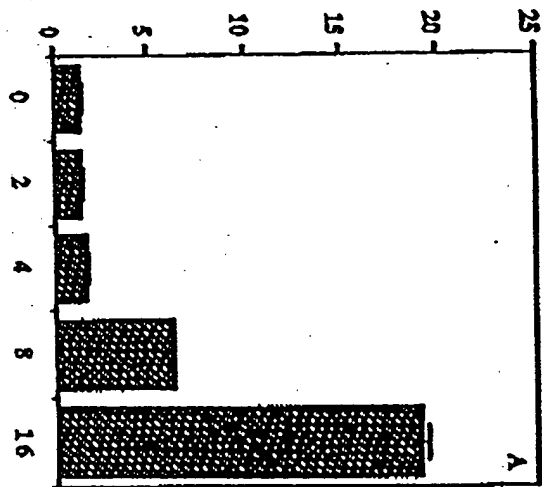
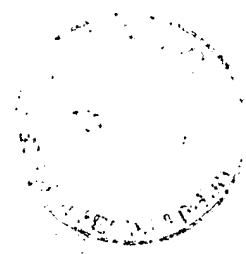


FIG. 57








Time (h)	0	0.5	1	2	4
					
Mixture					
Fold increase	1.0	0.8	0.8	1.3	1.5
					
Avicin D					
Fold increase	1.0	1.5	1.7	1.9	3.5
					
Avicin G					
Fold increase	1.0	3.5	4.7	6.3	8.4

FIG. 58

A

Time (min) 0 1 2 5 10 20
 → Cyt-c

B

Avicla G (μg/ml) 0 0.03 0.12 0.5 2 5
 → Cyt-c

C


Untreated
DEVD
zVAD-fmk
Avicla G
DEVD+Avicla G
zVAD-fmk+Avicla G
 → Cyt-c

FIG. 59

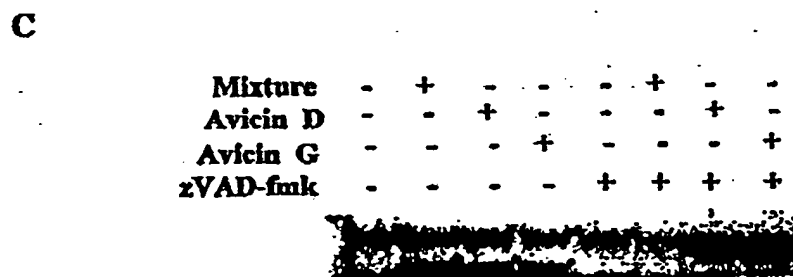
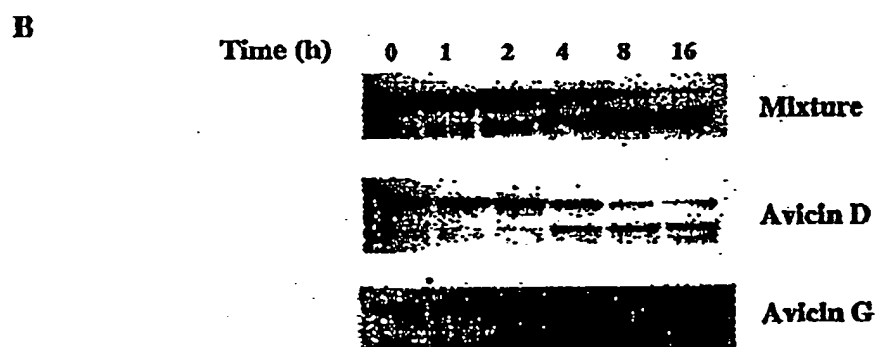
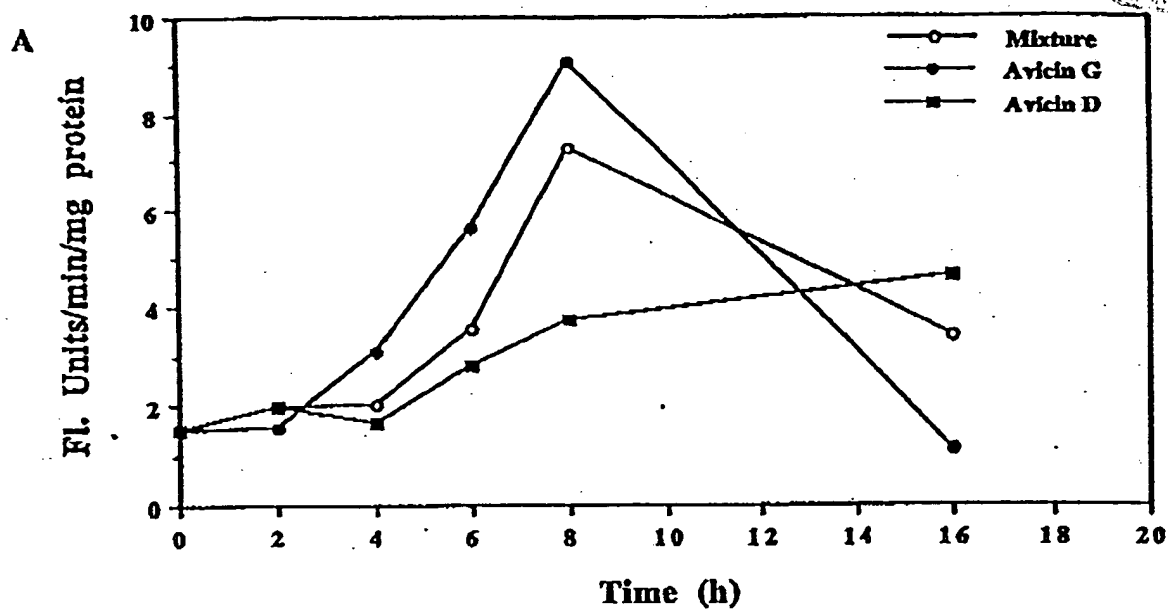


FIG. 60

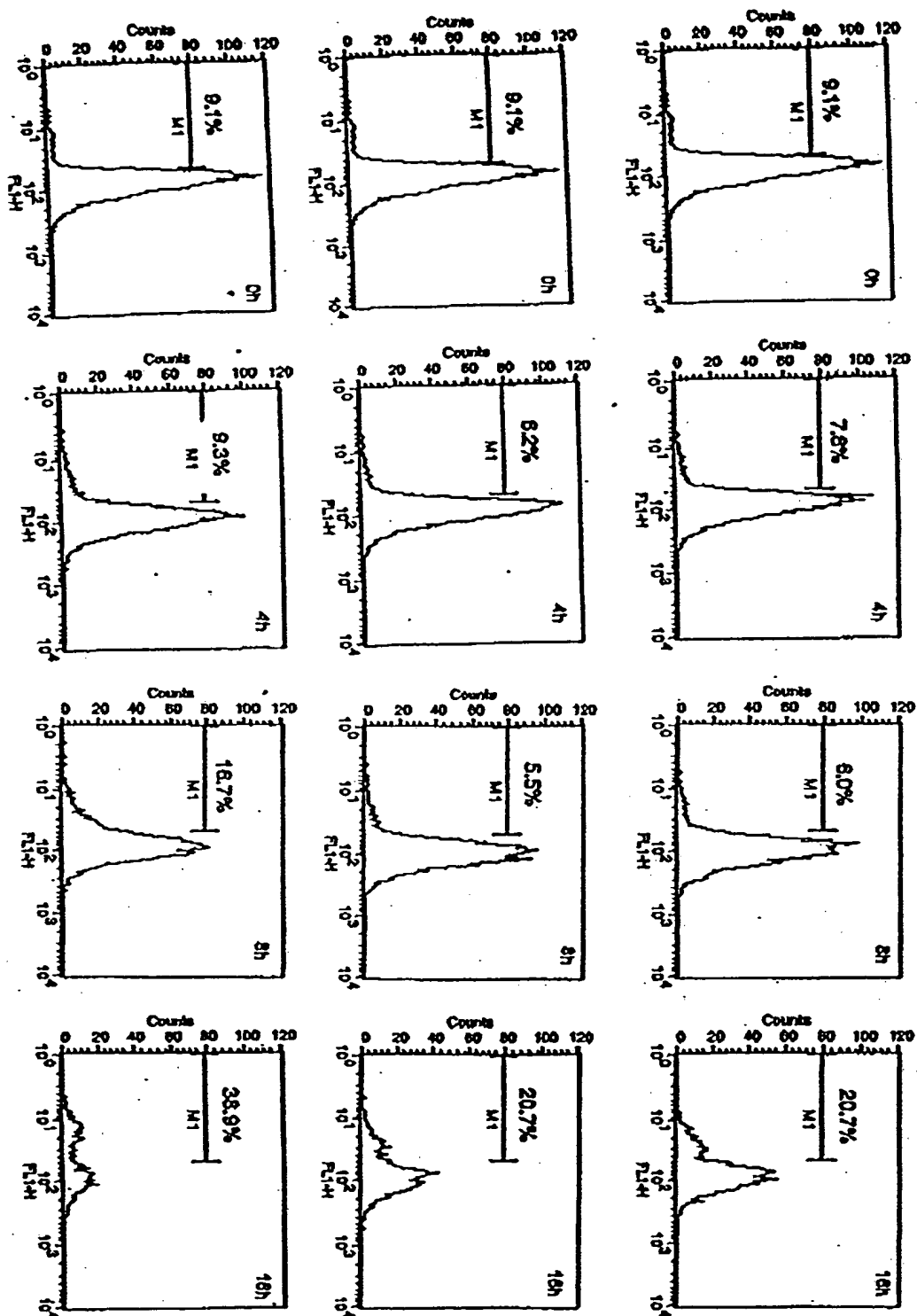
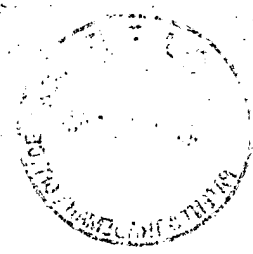


FIG. 61

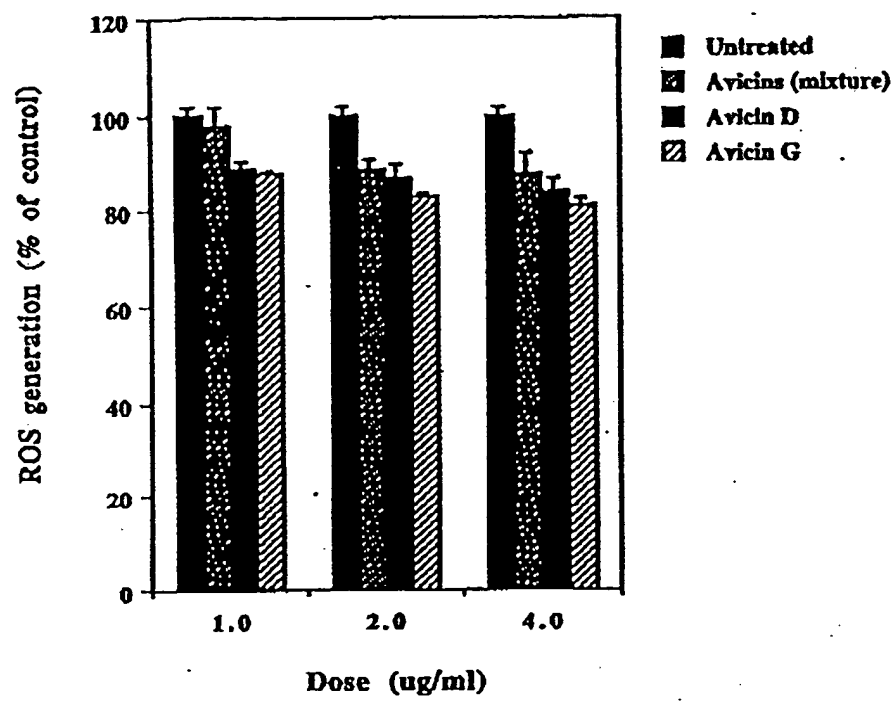


FIG. 62

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